## *Poster Group – Monday, September 26, 2005*

000120

### CAN PREOPERATIVE C125 LEVELS PREDICT LIKELY STAGE OF DISEASE AND LIKELIHOOD OF OPTIMAL DEBULKING IN OVARIAN CANCER

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**Objective:** Assess if preoperative Ca125 levels can predict stage & likelihood of debulking in ovarian cancer.
**Methods:** Ca125 assessed in 591 patients with ovarian cancers managed in Sheffield.
**Results:** (Table 1) Ca125 was raised (>35IU) in: 85% of all ovarian cancers; 89% of epithelial ovarian cancers (EOC); 100% of primary peritoneal tumours (PPT); 60% of borderline tumours. Ca125 levels increased from FIGO stage I to IV and were significantly higher in stage III/IV compared to stage I, and in patients with residual disease compared to those with no residual disease post-operatively ($p = 0.02$ Independent sample t-test). No significant difference in Ca125 was seen between optimally or sub-optimally debulked patients. Receiver operator curves (ROC) curves using Ca125 as a - diagnostic predictor, show good separation of stage I from stage II/III/IV disease and of patients with no residual disease from those with residual disease, with AUC (area under curve) values of 0.69-0.82. If Ca125 cut-off levels for predicting residual disease and stage II/III/IV disease are selected as 284IU & 205IU respectively, sensitivity of 71% and 74%, and specificity of 70% and 74% respectively are achieved.
**Conclusions:** Pre-operative Ca125 levels can be used as a predictor of patients likely to have residual disease and FIGO stage greater than stage I disease, with sensitivities and specificities of 70-74%. Ca125 cannot however accurately predict exact stage or likelihood of optimal versus sub-optimal debulking.

**Table 1: Ca125 levels with tumour type, FIGO stage and residual disease + Receiver Operator curve values using Ca125 as a diagnostic test separating stage & residual disease.**

| Tumour | Number of patients ( %) | Mean Ca125 (IU) | Median Ca125 (IU) |
|---|---|---|---|
| All Tumours | 591 | 1583 | 272 |
| 1: Epithelial | 412 (70%) | 1655 | 410 |
| Stage I | 100 | 519 | 75 |
| Stage II | 38 | 836 | 425 |
| Stage III | 201 | 2278 | 600 |
| Stage IV | 37 | 1621 | 960 |
| Stage unknown | 36 | | |
| 2: Borderline | 94 (16%) | 146 | 55 |
| 3: Peritoneal | 15 ( 2%) | 13311 | 743 |
| 4: Others | 70 (12%) | 576 | 121 |

| Residual disease after surgery | Number of patients ( %) | Mean Ca125 (IU) | Median Ca125 (IU) |
|---|---|---|---|
| Nil | 257 (53%) | 654 | 99 |
| 0.1-2cm ( Optimally debulked) | 124 (24%) | 1630 | 551 |
| >2cm ( Sub-optimally debulked) | 108 (22%) | 1648 | 739 |

| Receiver operator curves using Ca 125 as a test for separating : | Area Under Curve (AUC) | Ca125 Cut-off between groups | Sensitivity | Specificity | Positive Predictor Value | Negative Predictor Value |
|---|---|---|---|---|---|---|
| Stage I vs II | 0.69 | 116 | 65% | 64% | 35% | 86% |
| Stage I vs III | 0.82 | 245 | 76% | 76% | 83% | 68% |
| Stage I vs IV | 0.80 | 172 | 69% | 69% | 38% | 89% |
| Stage II vs III | 0.65 | 442 | 58% | 58% | 88% | 22% |
| Stage II vs IV | 0.64 | 440 | 58% | 58% | 57% | 60% |
| Stage III vs IV | 0.51 | 585 | 51% | 49% | 15% | 91% |
| Stage I vs II/III/IV | 0.80 | 205 | 74% | 74% | 87% | 58% |
| No Residual vs Residual disease | 0.77 | 290 | 71% | 70% | 69% | 73% |
| No Residual vs <2cm Residual | 0.75 | 258 | 67% | 67% | 50% | 81% |
| No Residual vs > 2cm Residual | 0.79 | 327 | 73% | 73% | 54% | 87% |
| <2cm residual vs > 2cm Residual | 0.55 | 604 | 54% | 54% | 51% | 58% |

000121

### BOWEL SURGERY IN OVARIAN CANCER- RISK FACTORS AND PROGNOSIS

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**Objectives:** To determine the likelihood of bowel resection in patients undergoing surgery for ovarian cancer, identify factors associated with increased risk and determine prognosis.
**Methods:** Data was collected prospectively and analysed from 842 patients with ovarian, managed in the Sheffield gynaecological cancer centre between 1985 and 2002. The study was a case control study comparing patients undergoing bowel resection with patients not needing bowel resection.
**Results:** (Table 1) Bowel resection was performed in 8.6% of patients. The risk of bowel surgery increased significantly ($p < 0.0001$ $\chi^2$ test) from 1st (5.8%) to 2nd operation (22%), with presence of bowel disturbance (21.9% versus 6.3% with no bowel disturbance), with FIGO stage III/IV disease (12.8% versus 2% for stage I/II) and Ca125 levels ≥2500 (12.9% versus 4.8% with Ca125 < 2500). There was no significant change in risk with other symptoms or factors. Overall 5-year all cause survival was 41%. Tumour histology, FIGO stage, postoperative residual disease and bowel resection were all prognostic factors. Bowel resection was associated with a significantly worse 5-year survival (14%).
**Conclusions:** Patients with bowel disturbance, Ca125 ≥ 2500, FIGO stage III/IV disease or undergoing second operations for ovarian cancer are at increased risk of bowel resection and should be selectively offered stoma marking and counselling. Bowel resection is associated with poor prognosis and should be performed only if it will result in optimal debulking or relieves imminent bowel obstruction.

Table 1: Percentage of patients undergoing bowel resection with presence or absence of one or more significant factor affecting risk.
Indicates only 1 factor assessed

| % of patients: Factor 1 / Factor 2 | | Bowel disturbance | | Operation number | | FIGO Stage | | Ca125 | |
|---|---|---|---|---|---|---|---|---|---|
| | | No | Yes | 1 | 2 | I/II | III/IV | <2500 | >2500 |
| Bowel disturbance | No | 6.3 | X | 4.8 | 19 | 2 | 11 | 4.5 | 6.5 |
| | Yes | X | 21.9 | 20 | 50 | 0 | 28 | 15 | 23 |
| Operation number | 1 | 4.8 | 20 | 5.8 | X | 2 | 9 | 3.7 | 12 |
| | 2 | 19 | 50 | X | 22 | 0 | 31 | 15.2 | 0 |
| FIGO Stage | I/II | 2 | 0 | 2 | 0 | 2 | X | 1.5 | 12.5 |
| | III/IV | 11 | 28 | 9 | 31 | X | 12.9 | 8.4 | 13.7 |
| Ca125 | <2500 | 4.5 | 15 | 3.7 | 15.2 | 1.5 | 8.4 | 4.8 | X |
| | >2500 | 6.5 | 23 | 12 | 0 | 12.5 | 13.7 | X | 12.9 |

000122

### ENDOMETRIAL CANCERS: EPIDEMIOLOGY, MANAGEMENT AND PROGNOSIS. SHEFFIELD CASE SERIES OF 664 PATIENTS

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**Objective:** To determine epidemiology, management and outcome of endometrial cancers managed in Sheffield.
**Methods:** Prospective case series of 664 patients.
**Results:** Age = 33-93years, mean = 65. 57% had medical co-morbidity: Hypertension = 46%; Ischaemic heart disease = 24%; Diabetes mellitus = 9%. Presenting symptoms: Postmenopausal Bleeding = 79%, inter-menstrual bleeding = 3%, vaginal discharge = 3.6%, menorrhagia = 6%, post coital bleeding = 2%, irregular bleeding = 1.5%, pain = 2.6%, Others = 2.8%. Symptom duration = 0-72 months. Investigations performed: USS = 55% (Abnormal in 92%; Endometrial thickness (ET) = 1.3-73 mm, mean = 16.9 mm. ET < 5 mm in 8.75%); Hysteroscopy = 72%; Pipelle = 48%; D&C = 35%; TCRE = 0.7%, 2.3% diagnosed after hysterectomy; biopsy of vaginal mass = 0.9%. Surgery performed in 96%: Abdominal hysterectomy = 89%; Radical hysterectomy = 5.5%; Vaginal hysterectomy = 2.5%; Subtotal hysterectomy = 0.3%; Exenteration = 0.3%; Bilateral salpingo-oophorectomy = 90%; LSO = 1.4%; RSO = 1.4%; Omentectomy = 5.6%; Omental biopsy = 0.5%; Pelvic lymphadenectomy = 4%; Pelvic node sampling = 2.7%.

Ascites was present in 5.4% & was positive of malignant cells in 32%. Washing taken in 98% & positive of malignant cells in 7%. Myometrial invasion: Nil = 4%, superficial = 18%, < 50% = 37%, 50% = 0.5%, >50% = 40%. FIGO staging: I = 68%; II = 16%; III = 14%; IV = 1.5%. Histology: Adenocarcinomas = 89.5%; Mixed Mullerian = 5.1%; Stromal sarcomas = 2.1%; Leiomyosarcomas = 1.5%; Adenosarcomas = 0.2%; Adenosquamous carcinomas = 0.2%; others = 1.5%. Of Adenocarcinoma: Papillary serous = 47.5%; Endometrioid = 37.5%; Clear cell = 12.5%; mixed cell type = 2.5%. Tumour grade: 1 = 52%; 2 = 29%; 3 = 19%. Adjuvant treatment: Nil = 65%; Radiotherapy = 32%; Chemotherapy = 1%; Hormonal therapy = 1.5%. 5-year survival: All uterine tumours = 56%; Adenocarcinomas = 61%; others = 33%. With FIGO stage I = 72%; II = 58%; III = 33%; IV = 29%.

**Conclusions:** Endometrial cancer is a disease of the elderly, presents mainly with PMB and at stage I, investigations have changed with time. It is managed mainly surgically and has a 5-year survival of 56%.

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## CERVICAL IMPEDANCE SPECTROSCOPY FOR SCREENING OF CIN: RESULTS OF A PROSPECTIVE STUDY OF 176 PATIENTS

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**Objective:** Assess performance of electrical impedance spectroscopy (EIS) in separating CIN from normal cervical tissue using the MKIII impedance probe.

**Methods:** Prospective observational study of 176 women referred to colposcopy with abnormal Pap smears. A pencil probe measured EIS from cervical epithelium. Colposcopy and probe positioning were video recorded to allow correlation between results from colposcopy, histopathology and EIS measurements. EIS derived parameters R,S,R/S,C and Fc were assessed in CIN and normal epithelium. The performance of the probe in identifying women with CIN was assessed.

**Results:** From Squamous epithelium to CIN1 and CIN2/3: R falls by 48-80%, S rises by 28-59%, Fc rises by 40-150% (Table 1). Tissues separated include (Mann-Whitney test $p < 0.0001$): CIN2/3 from squamous (R,S&Fc), mature metaplasia (R,S,C&Fc) and columnar (C); CIN1 from squamous (R&S),immature metaplasia (C&Fc), columnar (S,C&Fc); Squamous from immature metaplasia (R,S,C&Fc), mature metaplasia (R), columnar (R,S,C,Fc). ROC curves using parameters R,S,C,Fc & R/S for separating CIN1 & CIN2/3 from normal tissue types give area under curve values from 0.51-0.89 (Table 2). If the women were categorised on the basis of any impedance results for R/S of 0.64 as cut-off between classifying points as normal or CIN, then sensitivity = 66.3%, specificity = 49, PPV = 67.7% and NPV = 55% for detection of CIN are obtained.

**Conclusions:** The EIS MKIII probe has similar sensitivity and specificity to currently used screening tests in detecting CIN and is an exciting potential real time screening tool for CIN. Further work is needed to improve separation of CIN from immature metaplastic tissue, to improve the performance of the probe in clinical use.

**Table 1: Statistical data for parameters R (Ωm), S (Ωm), C ($\mu F m^{-1}$), Fc (Hz) and R/S in different Tissue groups.**

| Tissue type/ Medians | N | R(Ωm) | S(Ωm) | C($\mu F m^{-1}$) | $F_c$(kHz) |
|---|---|---|---|---|---|
| Squamous | 680 | 20.05 | 2.99 | 0.67 | 8.90 |
| CIN 1 | 39 | 8.49 | 3.67 | 0.80 | 12.79 |
| CIN2/3 | 178 | 3.99 | 5.88 | 0.49 | 28.69 |
| Columnar | 28 | 2.61 | 7.73 | 0.24 | 69.65 |
| Immature metaplasia | 79 | 3.48 | 5.81 | 0.40 | 40.41 |
| Mature metaplasia | 135 | 13.76 | 3.14 | 0.84 | 9.78 |

**Table 2: Area under the curve values of Receiver operator curves (ROC) separating high and low grade CIN from different tissue types.**

| Epithelium | High Grade CIN | | | | | Low grade CIN | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Parameter | R | S | C | Fc | R/S | R | S | C | Fc | R/S |
| Original Squamous | 0.88 | 0.83 | 0.63 | 0.79 | 0.89 | 0.78 | 0.70 | 0.58 | 0.63 | 0.77 |
| Columnar | 0.68 | 0.65 | 0.67 | 0.67 | 0.69 | 0.83 | 0.83 | 0.84 | 0.86 | 0.83 |
| Mature Metaplasia | 0.80 | 0.80 | 0.69 | 0.77 | 0.81 | 0.65 | 0.64 | 0.51 | 0.61 | 0.66 |
| Immature Metaplasia | 0.54 | 0.51 | 0.55 | 0.55 | 0.55 | 0.71 | 0.71 | 0.74 | 0.74 | 0.72 |

000124

## PAP CYTOLOGY SCREENING FAILURE: INFLUENCES OF THE PATIENT, PHYSICIAN, AND LABORATORY

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**Objectives:** 1. To identify and to rank the failures along the cancer care continuum that led to development of invasive cervical cancer (ICC). 2. To explore reasons for these failures.

**Methods:** Study subjects are women living in Montreal diagnosed with ICC between 1998-2004 (n = 120/year) and are identified through the Quebec Tumour Registry. Data describing the process of cervical cancer screening and diagnostic tests, treatments received for pre-invasive lesions, physician recommendations, and patient compliance with these recommendations are abstracted from hospital medical charts. Cytology labs are searched for similar data. Telephone interviews with subjects are conducted using a pilot-tested questionnaire. Demographics, Pap history, reasons for screening failure, names of attending physicians, and symptoms are collected during the interview. Further data is obtained from physicians' office medical files. The normal, equivocal, and low-grade Pap smears each subject had 5 years before final diagnosis are then retrieved from cytolology labs and reviewed by a cytologist.

**Conclusion:** Data will be used to explore the natural history of ICC in relation to the process of medical care provided within various health care settings. From this we will develop public health initiatives and policies aimed at health care providers, women, and the health care system in North American urban settings. This study will provide information that can be used for health policy to reduce the health disparities that occur, in terms of early prevention of ICC, particularly amongst women of a low socioeconomic status.

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## THE ROLE OF WT1 GENE IN THE CARCINOGENESIS OF UTERINE SARCOMAS

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**Background:** Wilm's tumor gene (WT1), localised on chromosome 11, encodes a transcription factor and is important in the carcinogenesis of several tumors. Recent studies demonstrated the frequent presence of WT1 immunohistochemically in endometrial stromal sarcoma (ESS) (n = 10) and carcinosarcoma (CS) (n = 10). The aim of this study was to confirm these results genetically and further explore the role of WT1 in uterine sarcomas.
**Materials and Methods:** After central review, 84 samples of tumoral tissue were selected (27 CS, 38 leiomyosarcomas (LMS), 18 ESS and 4 undifferentiated sarcomas (US)). Immunohistochemistry was applied to all samples (WT1 antibody, clone 6F-H2, DAKO, 1:400 dilution). Quantification of WT1-mRNA was performed with real-time PCR (RT-PCR) in 23 cases. WT1 protein was quantified on 12 frozen samples by Western blotting (cytoplasmic and nuclear separately).
**Results:** The results on WT1 positivity in different subsets of uterine sarcomas are presented the table below (n (%)).
**Conclusion:** Until now, the potential role of WT1 in the carcinogenesis of uterine LMS was unknown. Molecular data in the different subtypes of uterine sarcomas confirm involvement of WT1 in their carcinogenesis. Apart from a diagnostic importance, these data might be useful in the development of new treatment strategies for this aggressive entity.

| | CS | LMS | ESS | US |
|---|---|---|---|---|
| Immunohistochemistry | 12/27 (45%) | 29/38 (76%) | 6/18 (33%) | 3/4 (75%) |
| RT-PCR | 3/6 (50%) | 5/6 (83%) | 7/8 (88%) | 2/3 (66%) |
| Western blotting | 4/4 (100%)* | 3/3 (100%)* | 4/4 (100%)* | 1/1 (100%)* |

* More expression of cytoplasmic WT1 protein

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## THE VALUE OF [18F] FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN PLACENTAL SITE TROFOBLAST TUMOR

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Gestational trophoblastic disease (GTD) is rare. Placental site trophoblastic tumor (PSTT) is a rare form of GTD, specified by its lower sensitivity to chemotherapy and its lower production of human choriogonadotrophin (hCG). PSTT consists of intermediate trophoblasts, producing human placental lactogen (HPL). This hormone causes insulin resistance during normal pregnancy, leading to hypoglycemic and hyperglycemic conditions. Consequently, HPL could interfere with the sensitivity of [18F] fluorodeoxyglucose positron emission tomography (PET). Although 6 cases on the clinical use of PET in choriocarcinoma have been reported, the value of PET in PSTT remains unknown. The present case describes a 26-year-old woman, diagnosed with PSTT for which she underwent abdominal hysterectomy. Because of non decreasing hCG, PET-CT was performed, indicating residual and metastatic lesions of PSTT in lung, pelvis and para-aortal lymph nodes. Metastatic spread was confirmed histopathologically. Both the primary and metastatic tumor had a positive HPL staining. The patient received 18 cycles of EP-EMA (Etoposide-Patinol and Etoposide-Methotrexate-Actinomycin) followed by 11 cycles ME (Methotrexate-Etoposide). Tumor regression was confirmed by serial PET-CT. Although HPL might interfere with PET sensitivity, these findings suggest that PET is a valuable diagnostic tool in PSTT.

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## LUNG METASTASIS OF THE RECURRENT CERVICAL CANCER

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**Introduction:** Recurrent cervical cancer constitutes of the serious problems in the management of cervical carcinoma. One of the factors compounding the management of recurrent cervical carcinoma is the case of lung metastasis.
**Objective:** To identify response to therapy for recurrent cervical carcinoma in the lung.
**Methods:** This study was a historical cohort trial in the cases of recurrent cervical cancer in the lungs encountered between 1990 and 2004 at Dr. Cipto Mangunkusumo General Hopsital, Jakarta. Diagnosis and Therapy response of metastasis was made on the basis of radioimaging photos 90) (chest x-ray and CT Scan). Therapy regimen of PVB (cisplatinum 60 mg/m$^2$, vinblastine, bleomycin 15 mg/day 1.8), PC regimen (paclitaxel 150 mg/m$^2$ and carboplatin 300 mg/m$^2$).
**Results:** Therapy response was assessed clinically and radiologically. There were 22 cases of recurrent cervical cancer with lung metastasis, and 17 patients received PVB therapy. In terms of therapy response, partial response was found in 7 cases (41.17%). As many as 5 patients received PC therapy, and 4 cases (80%) showed partial clinical response. Mean duration of therapy response to complaint of cough was 7.8 months, and mean PC was 11.75 months. From these preliminary results, it was evident that regimen of paclitaxel-carboplatin/cisplatinum provided better response.
**Conclusion:** PVB regimen in recurrent cervical cancer in the lung provided partial response of 41.17%, while PC provided partial response of 80%.

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## PREMATURE OVARIAN FAILURE AFTER TREATMENT FOR HODGKIN'S LYMPHOMA

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**Background:** The purpose of this study is to determine 1. the effect of treatment for Hodgkin's lymphoma on ovarian function 2. the interventions to relieve postmenopausal symptoms.
**Methods:** 77 consecutive patients treated for Hodgkin's lymphoma stage I and II between 1989 and 2003 in the Rotterdam region were approached for this study. All patients had been treated in EORTC trials (H7, H8, H9). After stratification in three major treatment groups, type of agents and dosage of chemotherapy and/or radiotherapy were determined by randomisation in trials.
**Results:** After informed consent 66 patients filled in a questionnaire. After anti-tumour treatment 13 patients developed treatment related post menopause, 35 patients had a spontaneous cycle, and 18 patients could not be classified as they used hormonal contraception. Women who developed treatment related post menopause had a significant higher average age at the time they started treatment for Hodgkin's lymphoma than women who remained premenopausal ($p < 0.002$). Only 6 of these 13 women (46%) received hormonal substitution. In total, 21 women conceived after anti-tumour treatment, and 28 children were born. All pregnancies were the result of spontaneous conception.

**Conclusions:** The effect of anti-tumour treatment for Hodgkin's lymphoma on ovarian function is age dependent. In our study, this effect was proven by an odds ratio of 1.18 per year. There is a striking inconsistency regarding the management of ovarian protection during anti-tumour treatment. Protocols for assessment and management of loss of ovarian function after anti-tumour treatment should be developed and standardised.

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**RESEARCH THE EFFECTS OF HORMONE REPLACEMENT THERAPY WITH TIBOLONE OR ESTROGEN+PROGESTRONE ON VAGINAL LATE EFFECTS OF RADIOTHERAPY IN CERVICAL CANCER**

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**Objective:** To evaluate the effects of hormone replacement therapy (HRT) with tibolone (T) or estrogen+progesterone (EP) on vaginal late effects of radiation therapy.

**Materials and Methods:** A prospective, randomized, double-blinded, placebo-controlled study was designed. Between February 2004- March 2005, 48 patients (pts) with cervical carcinoma whose radiotherapy has been completed at least 6 months before randomization were accepted in the study. After informed consents of the pts were taken they were randomized T, EP and placebo (P) groups. To evaluate the sexual functions FSFI test, vaginal late effects SOMA-LENTS score, pathological changes vaginal smear tests were done in the beginning and every 3 months. To measure the vaginal volume and diameters vaginal imprints were taken first in the beginning and after 6 months.

**Results:** Age, histopathology and stage were homogenous between three groups. Vaginal imprint length, width and diameter were increased in HRT groups significantly. The difference in vaginal volume was higher in the EP group than in the T group. FSFI scores were improved in T group. SOMA- LENTS scores at 3 and 6 months were significantly higher when compared the beginning and P group scores. T group has significantly better scores when analyzed within and between groups. Pathologically, degeneration was reduced significantly at 6 month only in EP group.

**Conclusion:** HRT can be recommended pts treated for cervical cancer who is suitable and has vaginal late effects of radiation.

000130

**THE ACCURACY OF FROZEN SECTION DIAGNOSIS AT SURGERY IN PRE-MALIGNANT AND MALIGNANT LESIONS OF THE ENDOMETRIUM**

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**Objective:** The purpose of this study was to correlate the histological diagnosis made during intra operative frozen section examination with the final definitive histology made on paraffin sections. Study Design: Frozen section pathology results of patients with pre-op biopsy showing atypical hyperplasia or endometrial cancer (55 patients) were compared prospectively with paraffin section pathology findings. Those patients with curettage specimen showing atypical hyperplasia had intra operative frozen section to determine whether an invasive lesion was present and determine if these patients required pelvic lymphadenectomy. The patients who had curettage showing endometrial carcinoma had intra operative frozen section to identify poor prognostic pathological factors including histological type, grade, depth of myometrial invasion and cervical involvement.

**Results:** The correlation between frozen sections and paraffin histology for histological subtype was 94.5% (52/55), grade of differentiation 85.5% (47/55) and poorly differentiated tumours 85.7% (6/7). Depth of myometrial invasion was accurately diagnosed in 90.7% (49/54) while cervical involvement was detected in 87.5% (42/48). Of the 22 patients with atypical hyperplasia on curettage specimen who had intra operative frozen section, 14 patients had invasive malignancy, which was confirmed on both frozen section and subsequent paraffin section. The remaining 8 patients with a frozen section diagnosing atypical hyperplasia, 6 were confirmed on paraffin section while 2 had a small invasive lesion.

**Conclusion:** Intraoperative frozen section is a useful procedure to identify poor prognostic pathological factors as well as diagnosing endometrial cancer in patients undergoing hysterectomy for atypical hyperplasia on curettage.

000131

**GERM CELL TUMORS OF THE OVARY: A REVIEW OF 48 CASES**

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**Aim of the study:** To assess the response to therapy for patients with dysgerminomatous and non-dysgerminomatous germ cell tumors of the ovary.

**Method:** Forty-eight cases with germ cell tumors of the ovary seen at Kidwai Memorial Institute of Oncology, Bangalore, India between 2001-02 were studied.

**Results:** Eighteen patients had dysgerminoma, eight endodermal sinus tumor (EST), eight Immature teratoma, two embryonal carcinoma and 12 mixed germ cell tumors. Three patients with dysgerminoma and FIGO stage Ia had unilateral salpingo-oophorectomy (USO) and were kept under surveillance follow up. Forty-five patients received combination of bleomycin, etoposide and cisplatin (BEP regimen) either as neoadjuvant (NACT, 7 cases) or as adjuvant therapy (38 cases) following definitive surgery performed at Kidwai Institute or elsewhere. Forty-six patients achieved complete remission (CR). Two patients had progressive disease and could not be salvaged. All the patients with dysgerminomatous tumors (18 cases, 100%) achieved (CR) including three patients kept under surveillance. Twenty-eight of 30 (93.3%) patients with non-dysgerminomatous tumors achieved CR. Three patients (all EST) had recurrent disease following CR within six months, two of which were salvaged by second line chemotherapy consisting of etoposide, ifosfamide and cisplatin (VIP regimen).

**Conclusion:** As in our previous study (Bafna et al, Int J Gynecol Cancer, 11, 300-04, 2001) non-dysgerminomatous tumors fared slightly worse than dysgerminomatous tumors. Neoadjuvant chemotherapy followed by interval debulking was also effective in this small study.

000132

**STAGE III AND IV OVARIAN CANCER IN THE SOUTH WEST OF ENGLAND: 5 YEAR OUTCOME ANALYSIS FOR CASES TREATED IN 1998**

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This study evaluates the 5-year outcome data for the management of advanced ovarian cancer in the South West of England. Anonymised

data for 361 stage III and IV ovarian cancers registered between 1st January 1998 and 31st December 1998 were obtained from the central gynaecological tumour database. The following data were identified: age at diagnosis, FIGO stage, ASA grade, tumour differentiation, treating network and surgeon, amount of residual disease after debulking surgery, current life status and date of death if applicable. Survival analysis was performed using Kaplan-Meier crude survival for univariate analysis and multivariate analysis was performed by Cox regression. In our data the 5 year survival for patients with stage III was 16% and stage IV 10%. Survival analysis demonstrated that patients in whom the disease was debulked to less than 1 cm were more likely to be alive 5 years after diagnosis than those with a 2 cm residuum ($p < 0.0001$). There was no significant survival difference for those patients operated on by subspecialist surgeons despite these surgeons being twice as likely to achieve optimal debulking. Therefore, there must be other variables influencing survival apart from cytoreductive surgery. While there is near complete data collection about ovarian cancer surgery, our database on chemotherapy is incomplete. This is clearly crucial for a complete view of cancer care in our region.

000133

**REDUCING THE RATE OF POST MOLAR PERSISTENT GESTATIONAL TROPHOBLASTIC DISEASE THROUGH EARLY DIAGNOSIS AND TREATMENT**

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**Objective:** To analyze the clinical presentation of hydatiform mole cases in the recent years and to evaluate its effect on the time of diagnosis and the rate of persistent disease.

**Methods:** We reviewed charts of 68 consecutive cases of complete moles and 95 cases of partial moles admitted to two medical centers in Israel during the period 1998-2003, and analyzed the clinical features, mode of presentation and rate of persistent disease.

**Results:** 50.3% of hydatiform molar pregnancies were diagnosed by a routine early pregnancy ultrasound imaging while being asymptomatic, 33.8% and 62.1% of complete mole and partial mole respectively. The sonographic appearance was of a nonviable pregnancy in 38.9% and of suspected molar pregnancy in 61.1% of complete moles and 68.9% and 31.1% respectively in partial moles. Evacuation of the molar pregnancy occurred at a mean gestational age of $11 \pm 3$ weeks (mean $\pm$ SD) for both complete and partial moles. An overall rate of persistent disease was recorded in 12 of 163 (7.4%) patients. Persistent gestational trophoblastic disease was documented in 8 of 68 (11.8%) in complete moles and in 4 of 95 (4.2%) of partial moles.

**Conclusions:** Compared to historic controls, there is a shift in the presentation of complete and partial molar pregnancies. Higher rates of asymptomatic patients are diagnosed following an ultrasound examination demonstrating a nonviable pregnancy or an appearance suggestive of a molar pregnancy. This change leads to early termination of the pregnancy, with less associated complications and a reduced rate of persistent trophoblastic disease.

000134

**PERIOPERATIVE MORBIDITY AND MORTALITY OF GYNECOLOGICAL ONCOLOGIC SURGERY IN ELDERLY WOMEN**

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**Objective:** The study compares perioperative morbidity and mortality rates between elderly ($\geq$70 years old) and younger ($<$ 70 years old) patients, undergoing surgery due to ovarian or uterine cancer.

**Methods:** The study cohort consisted of 171 women who underwent explorative laparotomy due to uterine or ovarian cancer. Clinical data included patients' age, co-morbidities, chronic use of medications, body mass index ($kg/m^2$), past and current surgical procedures, surgical stage of the disease (by FIGO), histological type and number of dissected lymph nodes as confirmed by histological examination, optimal versus non-optimal debulking (defined as residual tumor of less than 1 cm), the occurrence of perioperative complications and postoperative hospital stay (days).

**Results:** 171 women were divided to 108 (63.2%) patients with uterine cancer and 63 (36.8%) patients with ovarian cancer. Women having uterine cancer were further subdivided to those $<$ 70 years old (72 women, 66.7%), and those $\geq$70 years old (36 women, 3.3%). Similarly, women with ovarian cancer were subdivided to those $<$ 70 years old (48 women, 76.2%), and those $\geq$70 years old (15 women, 23.8%). Excluding the occurrence of postoperative ileus and poorly controlled hypertension in the elderly subgroup of women with uterine cancer, the rate of early postoperative complications was similar between the two subgroups.

**Conclusion:** Chronological age by itself should not be a contraindication for the treatment of elderly women with gynecologic malignancy, since it is a poor predicting factor for perioperative morbidity.

000135

**THE ROLE OF SALVAGE SURGERY IN OVARIAN CANCER PATIENTS**

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**Purpose:** The aim of this study was the evaluation of value of salvage surgery in ovarian cancer patients.

**Material and Methods:** Between Jan 1996 and Jan 2002, 36 patients were treated because of ileus due to relapsed ovarian cancer. Two groups of patients were compared. The first group consisted of 21 women who were treated by using surgery. The second group of patients (N 15) was treated with conservative method. The FIGO stage in all cases was classified as III or IV. These were comparable group of patients according to age and performance status. The main differences between both groups were number of intestinal stenosis and willing to live. In case of 3 or more sites of stenosis, patients were qualified to conservative treatment.

**Results:** Within the group of surgical treatment, in 15 cases ileostomy was done. In other 6 cases gastrointestinal bypass was performed. In 19 patients chemotherapy was continued after surgical procegures. In this group of patients median time of survival was 9 months. In the conservative treatment group median survival was 3,2 months. No patients were treated with chemotherapy within 'the conservative group'. There was statistical difference in survival between both groups P = 0,003. Multivariate analysis confirmed that the main prognostic factors that influenced on survival were: histologic grade of tumor and effectiveness of surgery.

000136

**RECURRENCE AND FERTILITY IN WOMEN WHO TREATED WITH FERTILITY-SPARING SURGERY FOR OVARIAN TUMORS; A RETROSPECTIVE STUDY**

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**Objectives:** To assess the recurrence and fertility following fertility-sparing surgical management of ovarian malignancies.

**Methods:** 142 patients with ovarian tumors who underwent fertility-sparing surgery from 1991 to 2003 were evaluated from medical records of Ankara Etlik Maternity and Women's Health Teaching and Research Hospital.
**Results:** The mean age was 21.7 (13-42). The histological types were 56 (39.4%) germ cell tumors, 9 (6.33%) epithelial tumors, 15 (10.56%) sex cord stromal tumors, 62 (43.66%) borderline ovarian tumors. Clinic stages were involved of 87 (61.2%) early stage, 14 (9.85%) advanced stage and 41 (28.8%) unstaged. Among 142 patients, the fertility desire was in 53 patients (37.3%). 19 women had 23 pregnancies. 19 women had successful pregnancy with a total of 16 live births, 3 abortions, 3 unknown outcomes and 1 induced abortion. The recurrence observed in 11 (7.74%) patients. The mean of disease free survival was 21.6 months (6-69). Disease related death occurred in one patient. The mean duration of follow-up was 40.5 months (Range 1-126).
**Conclusions:** Fertility-sparing surgery for ovarian tumors should be considered for women in reproductive age group who desire preservation of fertility.

000137

**THE PREDICTIVE VALUE OF PREOPERATIVE CA 125 LEVEL FOR LYMPH NODE METASTASIS AND CLINICOPATHOLOGIC FEATURES AMONG ENDOMETRIUM CANCER PATIENTS**

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**Background:** The accepted treatment option of endometrium cancer mostly consists of hysterectomy with bilateral salpingo-oophorectomy, peritoneal cytological sampling, pelvic/paraaortic lymphadenectomy. The efforts to predict the pathological spread of the disease may contribute to select the suitable cases that selective lymphadnectomy or less aggressive surgery may be performed.
**Objective:** To evaluate the predictive value of preoperative serum levels of Ca 125 in patients with endometrial cancer in relation to clinicopathological parameters and lymph node metastasis.
**Material and Method:** A retrospective analysis of 215 consecutive endometrium cancer patients between January, 1992 and July, 2004 was performed. In all patients, total abdominal hysterectomy, bilateral salpingo-oophorectomy and washing cytology with complete pelvic/para-aortic lymphadenectomy was performed. The Mann–Whitney U, Kruskal–Wallis test and $X^2$ Fisher's exact test were employed to examine the effects of clinicopathological factors on serum Ca 125 levels. All data are expressed as median.
**Results:** The median level of serum Ca 125 was comparable among $\leq$50 and >50 years aged groups ($p > 0.05$). Also, no significant difference was noted when patients were classified according to histopathological stage, presence of high risk histology (non-endometrioid), lympho-vascular space invasion, cervical and adnexial involvement, pelvic/paraaortic lymph node metastasis and depth of myometrial invasion ($p > 0.05$). Of interest, median serum Ca125 level was significantly higher when tumor size was >2cm (18.8 vs 14.5 U/ml, $p = 0.01$), and washing cytology was positive (41.0 vs 23.5 U/ml, $p = 0.012$).
**Conclusion:** In contrast with earlier reports, the preoperative serum Ca 125 level was not significantly different in the presence of metastatic pelvic/paraaortic lymph node.

000138

**THE PREOPERATIVE PLATELET COUNT IS HIGHER IN ENDOMETRIUM CANCER PATIENTS WITH THE ADVANCED STAGE AND HIGH GRADE**

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**Background:** Although the exact mechanism is not known, the association between elevated platelet (PLT) counts and malignant neoplasia has been known since 1872. However, there is limited data whether there is a clear correlation between preoperative PLT count and prognostic factors of endometrium cancer.
**Objective:** To evaluate the predictive value of preoperative platelet count for clinicopathologic features of endometrium cancer.
**Material and Methods:** A retrospective analysis of 155 endometrium cancer patients between January, 1994 and July, 2004 whom were all treated with hysterectomy, bilateral salpingo-oophorectomy, complete pelvic/para-aortic lymphadenectomy and washing cytology. For univariate analysis the Mann–Whitney U test and Kruskal–Wallis test were employed. All data are expressed as median.
**Results:** No significant difference was noted when cases were classified according to the age (between $\leq$50 and >50 years aged groups), presence of non-endometriod histology, >1/2 depth myometrial invasion, pelvic/paraaortic lymph node metastasis and lenfovascular space invasion ($p > 0.05$). However, the PLT count was found to be higher in grade 3 patients both from grade 1 and 2 (316.500/ml vs 286.000 and 271.000, $p = 0.03$). Of note, advance staged (FIGO stage III and IV) group had increased PLT count when compared with early staged (FIGO stage I and II) group (309.000/ml and 273.500/ml respectively, $p = 0.004$).
**Conclusion:** High preoperative PLT count may reflect poor prognostic factors such as advanced stage and high grade histology in endometrium cancer.

000139

**THE CLINICAL VALUE OF PREOPERATIVE SERUM LIPID PROFILE FOR THE CLINICOPATHOLOGIC FEATURES OF ENDOMETRIUM CANCER**

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**Background:** Although the presence, nulliparity, obesity, diabetes mellitus and unopposed estrogen exposure are well known risk factors for endometrium cancer. However, there is paucity of data for the relation between endometrial cancer and dyslipidemia.
**Objective:** To evaluate the relation between preoperative serum lipid profile and clinicopathologic variables of endometrium cancer. Material and method: The clinicopathologic features of 70 endometrium cancer patients, whom were all treated with hysterectomy, salpingo–oophorectomy, pelvic/para-aortic lymphadenectomy and peritoneal cytology were examined. The Mann–Whitney U and Kruskal–Wallis tests were employed to examine the effects of clinicopathological variables on serum triglyceride (TRG), total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and very low density lipoprotein (VLDL) levels. All data were expressed as median.
**Results:** In patients $\leq$50 years of age, the serum VLDL (26 vs 32.9 mg/dl, $p = 0.008$) and TRG (129.5 vs 164.5 mg/dl, $p = 0.008$) were significantly lower. The lipid profile was similar when cases were classified according to the stage, presence of lenf node metastasis, positive cytology and larger than 2 cm of diameter tumor ($p > 0.05$). However, serum HDL was 56.5 and 45.5 mg/dl in the endometriod and non-endometriod histology groups, respectively ($p = 0.03$). Besides, both the VLDL (30 vs 7 mg/dl, $p = 0.03$) and TRG (150 vs 135 mg/dl $p = 0.03$) levels were found to be diminished when $\geq$1/2 myometrial invasion was observed. Also, all grade 3 tumors had lower serum HDL levels both from grade 1 and 2 (44.5 vs 57.5 mg/dl and 57.0, respectively, $p = 0.02$).
**Conclusion:** Lower preoperative serum lipid levels may reflect poor prognostic factors among endometrium cancer patients.

000140

**CAN A BIWEEKLY SCHEDULE REDUCE THE TOXICITY OF CAELYX? A PHASE-II STUDY OF HEAVILY PRETREATED PATIENTS WITH RECURRENT OVARIAN CANCER**

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Caelyx is a novel pegylated liposomal doxorubicin formulation and has been approved for the treatment of recurrent ovarian cancer (ROC). Palmar-plantar erythrodysthesia (PPE) is the dose-limiting toxicity and have an impact on patients' quality of life.

**Methods:** We performed a multi-institutional phase-II study to analyze the toxicity profile of PLD (20 mg/m$^2$/q 14d) in heavily pretreated patients with ROC.

**Statistic:** 2-Step-Design, in case of a positive first step (n = 26): >2 response + < 6 events of PPE (CTC Grade III/IV), a total number of 60 patients must be recruited; power: 80%, $p < 0.05$, based on a 10% reduction of PPE (95% CI).

**Results:** A total of 64 patients were recruited (10/2001-02/2004). 553 courses (median: 7, range: 1-35) were evaluable. Median age was 59 (38-81). Patients were generally heavily pretreated: 13 patients were in second-line, most of the patients were in third- or fourth-line. Ten patients were in fifth-line. Overall, the treatment was well tolerated. 30 patients developed skin toxicities: 18 patients with grade I, 9 with grade II and only 3 patients with grade III. These side effects occurred after a median of 5 courses. Heamatologic toxicity profile was favourable. Two patients achieved complete response, five patients partial response and 13 stable disease.

**Conclusion:** Despite the heavy pretreatment of the patients these results suggest that this new schedule seems to be an effective and well tolerated regimen, showing a low incidence of toxic skin reactions. Supported by ESSEX Pharma Germany.

000145

**UTERINE PAPILLARY SEROUS CARCINOMA ARISING OVER ENDOMETRIAL POLYPS: A DIFERENTIAL BEHAVIOUR?**

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**Objectives:** To analyze if Uterine Papillary Serous Carcinoma (UPSC) arising over endometrial polyps has different characteristics from focal or diffuse varieties arising over endometrial surface.

**Materials and Methods:** This study includes 43 patients with UPSC diagnosed between January 1998 and March 2005. 8 of them originated over an endometrial polyp, 8 were diffuse superficial forms, 10 had focal superficial lesions, 2 had a different origin and in 12 cases origin was unknown. In superficial patterns, overall survival was 21 months for focal and 17, 5 m for diffuse forms. Free disease interval was 15 m and 11, 3 m respectively. In UPSC over polyps, overall survival was 27, 3 m and free disease interval was 27, 3 m. For all 43 cases, mean overall survival was 22, 5 m and free disease interval was 16, 4 m.

**Conclusions:** Patients with UPSC arising over endometrial polyps seem to have a longer overall survival and increased free disease interval, though longer series are needed to determine prognostic utility of initial location and therapeutic alternatives in these cases.

000146

**DIFFERENT LEUKOCYTE RECRUITMENT ACCORDING TO THE MALIGNANCY POTENTIAL OF HIGH RISK HUMAN PAPILLOMAVIRUS-INDUCED CERVICAL LESIONS**

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**Objective:** High Risk (HR) HPV are the etiologic agents for cervical cancers. Infections by HR-HPV are generally cleared within a period of 8 to 13 months. Viral persistence that allows the progression of precancerous lesions to carcinoma is likely to depend on host factors. Among them, cellular immune responses targeted to the genital mucosa might be essential. We thus decided to characterize populations of immune cells in HR-HPV infected precancerous and cancerous cervical lesions.

**Methods:** Four biopsies from normal cervix, 4 CIN1 at high rate of regression, 5 CIN3 at high rate of progression, and 11 invasive carcinomas were analyzed. All lesions were HR-HPV positive and low risk-HPV negative. CD3, CD4, CD8 and CD45RO cells were identified by immunohistochemistry and their densities determined in the stroma and in the epithelium.

**Results:** CD4+ cells predominated in CIN1. While CD4+ and CD8+ cells were equally represented in CIN3, these cells aggregate as lymphoid follicles. Then, we observed a strong infiltration of CD8+ and memory cells in invasive cancers.

**Conclusions:** We identified a different distribution of immune cells in HR-HPV lesions that might be specific of their malignant potential. Accumulation of CD4+ cells in CIN1 is likely to be a regression marker. Whether the phenotype of immune cells may be consistent with an ongoing immune response in CIN3 and cancers, a poor distribution and/or functionality of these cells might explain their loss of efficacy to eliminate lesions.

000147

**PARTIAL TRACHELECTOMY: A NEW TREATMENT CHOICE FOR PERSISTENT OR RECURRENT HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA**

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**Objective:** Some women with persistent or recurrent disease after repeated conization for high grade cervical intraepithelial neoplasia (CIN) may desire to preserve uterus if not fertility. In such case a partial trachelectomy may become treatment of choice for them. We undertook this prospective study to determine examine the feasibility of partial trachelectomy as a treatment choice for persistent or recurrent high grade CIN.

**Methods:** Twenty premenopausal women with persistent or recurrent high grade CIN after initial LEEP and repeated conization refused hysterectomy, thus elected to undergo excision of vaginal portion of uterine cervix under general anesthesia in a tertiary university-affiliated medical center. High risk human papillomavirus (HPV) detection was done before initial loop electrosurgical excisional procedure (LEEP) and 3 months after partial trachelectomy. Follow-up PAP smear and colposcopy were done every 3 months during the first 2 years. If both exminations were negative, they were changed to yearly follow-ups.

**Results:** The out-patient procedure is simple and takes only 6.5 minutes in average. High risk human papillomavirus (HPV) were eradicated after procedure in all cases. During an average follow-up of 48 months, no recurrent dysplasia was observed.
**Conclusion:** Partial trachelectomy is a reasonable alternative treatment choice for those who suffer persistent or recurrent CIN, and desire to preserve their uterine corpi.

000148
**NERVE SPARING RADICAL HYSTERECTOMY AND BLADDER FUNCTION**
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Radical Hysterectomy is the recommended treatment for patients with early stage cervical carcinoma. Constipation, loss of bladder sensation, incomplete emptying and voiding difficulties are common after the operation. We attempted to preserve the autonomic nerve supply to the bladder during radical hysterectomy and conduct urodynamic study to assess the result. Twenty five stage 1B to 2A cervical carcinoma patients had urodynamic study before the radical hysterectomy. Intra-operatively, the hypogastric nerves were identified, dissected off the genital tract before parametria were divided and followed to the bladder. (A video can be displayed to show our technique). Bladder training commenced 7 to 10 days after surgery and suprapubic catheter was removed when residual urine volume was below 150 ml. Urodynamic study was then performed within 2 weeks. Fifteen patients had urodynamic study before and after the surgery and were included in the analysis. The median age of the patients was 41. The median operative time was 240 minutes and the median blood lost was 800 ml. We have found no change in the volume of first sensation to void (162 vs 173 ml) and urine flow rate (16 vs 15.6 ml/sec) before and after the operation. However, there is a significant increase in the residual urine volume after surgery (19 vs 166 ml). Our technique appears successful in preserving the sympathetic nerve supplies but less so the parasympathetic nerves supplies to the bladder. This explains the insignificant change in bladder sensation and flow rate but the increase in residual volume.

000149
**HUMAN PAPILLOMAVIRUS GENOTYPING BY HPV DNA CHIP IN KOREAN WOMEN**
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A recently developed HPV DNA chip test is a polymerase chain reaction (PCR) based microarray system that enables the rapid and easy detection and genotyping 15 high-risk and nine low-risk HPV types at once. In 2,361 women who were tested for HPV types by HPV DNA chip, cervical Thin Prep cytology and biopsy were also performed. High-risk HPV type was identified as positive in 29.1% of the 482 histologically confirmed normal samples and in 86.1% of the 609 samples of cervical intraepithelial neoplasia(CIN) and carcinoma. HPV-16 (41.8%) was the most prevalent type in samples with CIN II/III. The next common types were HPV-58 (16.7%), HPV-33 (10.8%), and HPV-31 (7.7%) in CIN II/III. These four types occupied 77.0% of the samples with CIN II/III. Among the 550 cases confirmed CIN II/III, carcinoma in histology, the rate of diagnosing HSIL or carcinoma in liquid based cytology was 83.5% and the detection rate of positive high-risk HPV in HPV DNA chip test was 86.5%. The prevalent HPV genotypes also provide valuable information about the development of vaccine, which was suitable for preventing cervical carcinoma in Korean women.

000150
**DETECTION OF HPV DNA AND MOLECULAR ANALYSIS OF CELL CYCLE GENES IN ABNORMAL, LIQUID BASED CYTOLOGICAL, SAMPLES FROM THE UTERINE CERVIX**
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**Aim:** Carcinogenesis in cervical cancer is a multifactorial process. In order to investigate the correlation of HPV types with cell cycle genes we examined cytological samples with epithelial atypia of different degrees.
**Methods:** Thin prep test was performed in 348 samples with ASCUS, LgSIL and HgSIL. In each case DNA extraction and PCR assays were carried out for β-globin, GP5+/GP6+ and HPV 6/11/16/18/31/33. 162 GP5+/GP6+ samples (51 ASCUS, 98 LgSIL, 13 HgSIL) were randomly selected for molecular analysis and subsequently submitted to RNA extraction, RT-PCR and Multiplex PCR for p53, bag, c-myc, bad, bax and bim. Statistical analysis was done using Pearson Chi square and Fisher's exact test.
**Results:** Distribution of HPV genotypes revealed that HPV 11 (38,5-48%) and HPV18 (33,3-38,5%) were more commonly expressed in this sample of Greek women while HPV 16 was identified in 53,6% of HgSIL. HPV 6 was not uncommon (20,4-30,8%) and less than 10% of all lesions expressed HPV 31 and 33. Anti apoptotic genes (bag, bcl-2) presented intermediate (17,6-33,7%) and high (41,2-76,9%) levels of expression respectively in all levels of cytologic atypia. C-myc oncogene showed increasing levels of expression 22% vs 42% vs 76% in ASCUS, LgSIL, HgSIL respectively while bad, bax, bim, p53 showed low expression.
**Conclusion:** There was no statistically significant correlation of low or high grade HPV types to cell cycle genes at the different cytological abnormalities examined. However there was a trend of rising bcl2 and c-myc expression with increasing level of atypia.

000151
**FERTILITY-SPARING TREATMENT FOR EARLY STAGE ENDOMETRIAL ADENOCARCINOMA**
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**Introduction:** Endometrial carcinoma (EC) is a disease that affects mainly peri- and postmenopausal women. It is relatively rare in women under 40. The standard therapy for this malignancy is a total hysterectomy, bilateral salpingo-oophorectomy, retroperitoneal lymph node sampling and peritoneal fluid cytology. We evaluated the outcome of conservative treatment of young women with EC.
**Materials and Methods:** Between September 2001 and July 2004 five premenopausal patients were treated with hysteroscopic resection of the EC, the endometrium near the lesion and of the myometrium under the lesion followed by megestrol acetate (160 mg/day) for six months as. Inclusion criteria were: age younger than 40, nulliparous, confirmed EC with grade 1 differentiation, presence of progesterone receptor, absence of myometrial invasion or extrauterine spread by vaginal ultrasound and magnetic resonance imaging and a strong desire to preserve fertility potential.
**Results:** Average age at diagnosis was 33 (range 27 to 39). All patients had an initial response after 3 months from the start of the conservative treatment. Median follow-up time was 14 months (range 9 to 45).

None of these patients developed recurrent disease during the follow-up time. Two patients gave birth at 39 weeks of gestation. After counseling, 3 out of 5 patients declared they were unwilling to undergo hysterectomy after childbearing while the remaining two would accept surgery after at least one successful pregnancy.
**Conclusion:** We think that these results indicate that this treatment strategy is feasible in young women with early well-differentiated EC who have a strong desire to preserve fertility potential.

000152
**WHICH IS THE BEST TECHNIQUE FOR ENDOMETRIAL SAMPLING? ASPIRATION (PIPELLE) VERSUS DILATATION AND CURETTAGE (D&C)**
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**Objective:** The aim of this study is to assess the diagnostic accuracy of two endometrial sampling technique (Pipelle and D&C) by comparing histologic findings with this techniques with those obtained by after hysterectomy.
**Material and Methods:** The study was conducted prospectively and we analyzed endometrial sampling results of 422 patients, and 302 out of 422 had abnormal uterine bleeding. Pipelle and D&C was performed within two weeks before hysterectomy. One hundred and twenty-four patients had pipelle results before hysterectomy and D&C was the biopsy technique before hysterectomy for 98 patients.
**Results:** Insufficient material rate for diagnosis were 2% and 6% for D&C and Pipelle, respectively. Complete histopatologic identical results were obtained 70% between D&C and hysterectomy. The same ratio was 64% for pipelle. Sixty percent of endometrial hyperplasia and 75% of high grade lesions were diagnosed with pipelle. However, only 23% of focal lesions were established with this technique. D&C diagnosed 67% of hyperplasia, 75% of high grade lesions and 37% of focal lesions. NPV and PPV of pipelle for focal lesions and high grade lesion were 78%, 99% and 43%, 100%, respectively. With respect to D&C, NPV and PPV were 80% and 76% for focal lesions. The same results for high grade lesions were 98% and 100%.
**Conclusion:** Both D&C and Pipelle are inadequate diagnostic and therapeutic tool for focal endometrial lesions. However, diagnostic power of pipelle are similar those of D&C. So, endometrial sampling with pipelle is an acceptable technique for global endometrial pathology.

000153
**MANAGEMENT OF ADOLESCENT OVARIAN MALIGNANCIES-A CONCEPTUAL DILEMMA**
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**Objective:** To study the clinicopathological presentation, treatment approach adopted and the treatment outcome of those Adolescent girls presented with Ovarian Malignacies were reviewed.
**Patients and Methods:** A retrospective analysis of the 1733 patients with ovarian Malignacies revealed 156 [9%] patients with Adolescent ovarian Malignancies between January 1982 & September 2004. All these patients were investigated, staged & treated according to the guidelines of FIGO. The previous surgical details & slides were reviewd by the institute pathologist. The data was analysed by using chisquare database.
**Results:** Majority of them belong to Germ cell tumor [78.2%] and less common is Epithelial ovarian cancer [16%], and stromal tumor [5.8%]. Most of them presented with inadequate previous surgery [88.2%] and all of them were subjected to adjuvant chemotherapy. 68.5% of them presented with advanced stage, 77.9% were alive without disease, 12.8% of them progressed, 9.35% of them succumed despite of the treatment. The followup ranged between 10 months to 168 months [medain 38.6 months].
**Conclusion:** This study indicates that the Adolescent girls presenting with Ovarian malignancy should be treated with conservative surgery followed by optimal adjuvant chemotherapy. However the relapsed & nonresponders requires judicious management.

000154
**INDUCTION CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER—A THERAPEUTIC DILEMMA?**
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**Objective:** To assess an alternative treatment approach for those patients unfit/unsuitable for surgery with Advanced Epithelial Ovarian Cancer and to study the quality of life issues in patients received the Neoadjuvant chemotherapy.
**Patients and Methods:** The records of 1733 Ovarian cancer patients presented at the Department of Gynaecological Oncology between January 1982 & September 2004 revealed 913 patients with advanced Epithelial Ovarian cancer. The Diagnosis was cofirmed either with histology or Cytology. Those patients unfit/unsuitable for surgery [n = 863] were subjected to two-three courses of Platinum/Taxol based Neoadjuvant chemotherapy and the clinical response was assessed at two-three weeks interval, & Interval Debulking surgery was performed in those patients responded to chemotherapy. The data was analysed by epichisquare database.
**Results:** The median age of the patients was 47.38 years. Majority of the patients showed complete or partial clinical response [84.3%], less than 10% had stable disease, & less 5% had meatastaic Adenocarcinoma from other sites. Optimal Cytoreduction was feasible in 88.4% of patients during Interval debulking surgery avoiding the extensive bowel resection & aggresive surgical pocedures. Quality of life was comparatively improvesd particulary in elderly patientsith with low performance status. However, the Progression free interval & survival benefits seems to be similar to that of the primary Cytoreductive surgery.
**Conclusion:** The present study confirms that the Induction chemotherapy is an alternative prudent option of treatment in patients unfit/unsuitable for primary surgery for Advanced Epithelial Ovarian cancer. It has definetely improved the quality of life & reduced the operative morbidity & mortality in selected group of patients with advanced disease.

000155
**LEVONORGESTREL INTRAUTERINE SYSTEM (MIRENA) AS PRIMARY TREATMENT FOR WOMEN WITH EARLY ENDOMETRIAL CANCER**
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**Background:** Intrauterine progesterone therapy potentially provides a simple alternative treatment for women with early endometrial cancers who are at high risk for surgery.
**Case Reports:** Five women with Stage I grade 1 endometrial adenocarcinoma with positive progesterone receptor were primarily treated with levonorgestrel intrauterine system. All were assessed to be in American Society of anaesthesiologists risk class IV and thus considered at high risk for perioperative complication. After insertion of mirena intrauterine system one woman (20%) had histological regression of disease within 6 months. Two of four women who did

not respond to treatment subsequently had hysterectomy, which showed endometrial cancer with myometrial invasion.
**Conclusion:** This report raises doubts about the effectiveness of intra uterine progesterone therapy as a definitive alternative for the treatment of early endometrial cancer. However, this option may offer an interim measure whilst co-morbid conditions are stabilised before definitive conventional treatment.

000156

**NEOADJUVANT CHEMOTHERAPY WITH PACLITAXEL, IFOSFAMIDE AND CISPLATIN IN LOCALLY ADVANCED CERVICAL CANCER: PHASE II TRIAL**

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**Purpose:** Neo-adjuvant chemotherapy (NACT) followed by radical surgery (RHND) represents an alternative to radiotherapy in locally advanced cervical cancer, with encouraging results as survival rate and pathologically confirmed response rate. Aim of this study was to evaluate effectiveness and toxicity of paclitaxel, cisplatin and ifosfamide (TIP) as NACT in cervical cancer.
**Patients and Methods:** From May 2002 to October 2004 33 stage IB2 to IIB cervical cancer patients were treated with TIP regimen; Paclitaxel: 175 mg/m$^2$ day 1, Ifosfamide: 5 gr/m$^2$ day 2-3 with Mesna, Ciplatin: 50 mg/m$^2$ day 1, every 3 weeks x 3. After 3 weeks from the end of NACT pts were submitted to type 3 RHND.
**Results:** 30/33 enrolled patients were evaluable for response and toxicity to NACT. Seven obtained a clinical complete response, 22 a partial response, 1 was stable, with an overall response rate of 97%. After RHND pathological CR were 23%, pPR 77%, while only one patient with stable versus progressive disease at the end of chemotherapy was not operated. Toxicity: grade 3 and 4 neutropenia was registered in 29% and 55% of patients respectively, grade 1 and 2 anaemia in 68% and 29%. Sixteen patients were treated with G-CSF. The median follow-up is seven months (range 1-59). The 3 years disease free survival rate is 62%.
**Conclusion:** In this experience NACT with TIP followed by radical surgery seems to be a very active treatment for locally advanced cervical carcinoma with acceptable toxicity.

000157

**CHEMORADIATION AS A SPHINCTER SPARING TREATMENT FOR VULVAR CANCER**

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**Objective:** To evaluate the role of chemoradiation as a sphincter sparing option for advanced/recurrent vulvar cancer.
**Methods:** From October 1997 to July 2003, 24 patients with locally advanced (n = 16) or recurrent (n = 8) diseases were selected for sphincter sparing therapy. The median age was 65 years (range 25-80 years). Biopsy-proven vulvar cancer (squamous, n = 22, adenocarcinoma, n = 2) were staged according to the FIGO (stage II, n = 4; stage III, n = 17; stage IV, n = 3). All patients received external radiation to a dose of 45 Gy (45-50, 4 Gy) to the primary and regional lymph-node areas followed by electron boost (10-20 Gy) to the vulva and clinically positive nodes or vulvar interstitial brachytherapy (20 Gy). Chemotherapy consisted of platinum (n = 16) or mitomycin-C (n = 8) based regimens.
**Results:** All patients reached initial complete clinical response. With a median follow-up of 32 months (4,4-63,6 months), 6 patients (25%) had a recurrence (5 local and 1 regional). The 2-year overall survival was 85% and the disease-free survival was 78%. Acute toxicities included urinary symptoms (G1 in 25%, G2 in 70,8%, G3 in 4%), diarrhea (G2 in 70.8%, G3 in 29.2%), perineal desquamation (G2 in 54.2%, G3 in 45.8%) and febrile neutropenia (12%).
**Conclusion:** Definitive chemoradiation is an effective option for advanced or recurrent vulvar cancer allowing organ and sphincter preservation. Further follow-up is required to determine the long-term outcome.

000158

**COMPARISON OF E-CADHERIN EXPRESSION IN SQUAMOUS CELL CARCINOMA (SCC) AND CIN 3**

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**Background:** E-cadherin (E-cad), a calcium dependent intercellular adhesion molecule, is important in cell growth and differentiation. Adhesion between cells is thought to decrease as cancers develop and disseminate. Therefore, E-cadherin is an important cellular adhesion molecule for the development and metastasis of malignancies.
**Objective:** To compare E-cadherin expression in CIN 3 and SCC of the cervix.
**Material and Method:** E-cad expression was analysed in surgically treated stage IB women with SCC and outpatients treated women with CIN 3, using commercially available polyclonal antibodies on Formalin-fixed, paraffin-embedded tissues. Patients were divided into two groups arbitrarily Group1: E-cad expression $< 50\%$, Group 2: E-cad expression $>50\%$. Statistical analysis was performed using Chi-square test and t test. Survival of the patients was compared by Kaplan-Meier analysis. Multivariant analysis was performed by Logistic Regression analysis. $P < 0.05$ was considered statistically significant.
**Results:** There were 40 patients in SCC group while there were 18 patients in CIN3 group. There was no significant differences with respect to age of both groups ($p > 0.05$). Other clinical variables were not significantly different among groups. Significantly lower expression of E-cad was observed in SCC group when compared with CIN group (62.5% vs. 22.2%, $p = 0.005$). Furthermore, intensity of E-cad staining was significantly lower in SCC group compared with CIN3 (59.5% vs. 16.7%, $p = 0.003$).
**Conclusion:** Loss of E-cadherin expression may have an important role in development of invasive SCC from preinvasive cervical neoplasias. Reduced E-cad expression may be incorporated into management and follow-up of preinvasive cervical neoplasias.

000159

**THE ASSOCIATION OF CATHEPSIN D EXPRESSION AND CLINICAL PROGNOSTIC FACTORS IN ENDOMETRIAL ADENOCARCINOMA**

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**Background:** Cathepsin D (CathD) is a lysosomal aspartyl protease secreted by normal and malignant cells. It is considered to be involved in breakdown of the extracellular matrix. Overexpression of CathD in several types of carcinoma in women appears to be associated with a poor clinical course. The expression of CathD has not been studied widely in endometrial adenocarcinoma. The aim of the present study was to determine the association of CathD expression and established prognostic factors in endometrial carcinoma.
**Materials and Methods:** The immunohistochemical expression of CathD was performed in paraffin embedded tissue from the patients

with endometrial carcinoma grade I (n = 35), grade II (n = 44), grade III (n = 25). The association between CathD and established prognostic factors was investigated.
**Results:** Of 84 tissue specimens, 51 (60.7%) showed a positive reaction for CathD. A significant correlation between CathD and histological grade was found ($P < 0.05$). The expression of CathD-positive increased with the size and myometrial invasiveness of the primary tumor ($p < 0.01$). Patients with vessel invasion and pelvic lymph-node metastasis had a higher incidence of CathD-positive staining than patients without these findings ($p < 0.05$). A favorable prognosis was obtained in CathD-negative cases in comparison with positive cases ($p < 0.01$). The expression of CathD in stromal cells was associated with lymph node positivity ($p < 0,05$).
**Conclusion:** The association of CathD expression with tumor differentiation and myometrial invasiveness may show promise as a clinically useful adjunct to prognosis assessment and the planning of therapy in the patients with endometrial adenocarcinoma.

000160

**CA125 LOCALIZES TO DIFFERENT INTRACELLULAR ORGANELLES IN DIFFERENT OVARIAN CANCER CELL LINES**

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**Objectives:** MUC16, the gene coding for the CA125 glycoprotein has been identified, and the intra-cytoplasmic domain of MUC16 is thought to have a role in cell signaling. It has been shown that MUC1 localizes to the mitochondria in colon cancer cells and has a role in resistance to chemotherapy. We set out to define the localization pattern of MUC16 in ovarian cancer cells.
**Methods:** Two ovarian cancer cell lines were used, OVCAR3, which secretes CA125, and SKOV3, which does not. The carboxy-terminal domain of MUC16 tagged to GFP was transfected into both cell lines using an expression vector. Both cell lines were also tested for mitochondria using Mitotracker. Confocal microscopy was used to determine localization of the GFP tagged MUC16 relative to the distribution of mitochondria in SKOV3 and OVCAR3 cells.
**Results:** In the OVCAR3 cell line, GFP tagged MUC16 localized preferentially to the mitochondria and to the cell membrane, whereas in the SKOV3 cells GFP tagged MUC16 was found to distribute diffusely in the cytoplasm and did not localize to either mitochondria or membrane.
**Conclusion:** Different ovarian cancer cell lines express CA125 in a different manner and process the glyco-protein differently. These differences may account for the differing sensitivity to chemotherapy among ovarian cancer cell lines in-vitro and might be relevant for in-vivo sensitivities also.

000161

**HPV AND P53 EXPRESSION IN OVARIAN CARCINOMA**

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**Objectives:** Human papillomavirus is the causal factor for cervical cancer. However, the role of HPV infection in ovarian cancer is unclear. This study aimed to determine the presence of human papillomavirus (HPV) in ovarian cancer tissues along with the expression of tumor suppressor gene p53. We also investigated any possible association of HPV with p53 gene mutations in ovarian carcinoma.
**Methods:** Archived human ovarian cancer tissues (n = 40 cases of epithelial ovarian cancer) embedded in paraffin blocks were used. Controls are 32 non-malignant ovarian tumor tissue blocks. In situ hybridisation (ISH) and immunohistochemistry (IHC) were used to detect the presence of HPV and p53 expression respectively.
**Results:** Of the total, 37.5% (n = 15) of malignant and 28.1% (n = 9) of benign ovarian tumors were positive for HPV (OR: 1.5 CI: 0.5-4.1, p = 0.4). The difference was not statistically significant. However, p53 was detected in 72.5% (n = 29) of malignant cases compared to 37.5% (n = 12) of benign cases (OR: 4.3 CI: 1.6-11.9, p = 0.003). Furthermore, a positive correlation between HPV and p53 expressions in ovarian cancer tissue samples was detected (r = 0.47, p = 0.001).
**Conclusions:** HPV seems to be not a major component in the development of ovarian carcinoma, nevertheless HPV positivity seems to contribute to the pathogenesis in at least some ovarian carcinoma cases by way of interaction with tumor suppressor p53.

000162

**ABNORMAL UTERINE BLEEDING IN EPITHELIAL OVARIAN CARCINOMA: A CASE CONTROL STUDY**

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**Objective:** The goals of this study are collecting the data about abnormal bleeding in patients with Epithelial Ovarian Carcinoma [EOC] at diagnosis and the previous 12 months and comparing the data to menstrual pattern in women referring to primary care clinic.
**Methods:** This is a case-control study in Vali-Asr hospital from 1995-2004.The epidemiologic data and menstrual pattern of 254 patients with EOC compared with 297 healthy women from primary care clinic in control group.
**Results:** Of 254 EOC, 30 had borderline tumors, 90 had early stage (I, II) and 164 had advanced (III, IV) invasive disease. Twenty seven percent of cases had some type of abnormal bleeding compared with 16% in control group. Time interval between first episodes of abnormal bleeding to diagnosis ranged from 2-5 months. Post menopausal bleeding in EOC patients was 2 times more than control group.
**Conclusion:** Earlier diagnosis of EOC may be possible if women and physicians recognize the importance of vague long-standing symptoms including abnormal bleeding in this group of patients.

000163

**AGE AND RESULTS OF TREATMENT OF ATYPICAL GLANDULAR CELLS**

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Glandular atypia in Papanicolaou smears from postmenopausal women can be the result of artifactual alterations such as drying artifacts and inflammatory changes or may represent a squamous or glandular, preneoplastic or neoplastic process. We studied 989 patients treated by large loop excision procedure (LLEP) for abnormal cervix smears at Brazilian National Cancer Institute between January 1999 and September 2003. Eighty six patients having atypical glandular cells (8.7%) were reviewed and corresponding final histological diagnoses were further evaluated, the mean age of the patients was 38.9 (15 to 65 years). The results of hystopatological findings were: to patients under 40 years old, the hystopatological finding confirmed cervicitis to 18% of patients, LSIL 18%, HSIL 46%, adenocarcinoma 6% and squamous cell carcinoma 12%. Comparably, forty aged and older patients had hystopatological finding: cervicitis to 19% of patiens, LSIL 17%, HSIL 50%, adenocarcinoma 8% and squamous cell carcinoma 6%. Differing of literature, there were no significant differences of hystopatological findings for age adjustment.

000164

**USEFULNESS OF HUMAN PAPILLOMAVIRUS TESTING IN THE FOLLOW-UP OF PATIENTS WITH HIGH GRADE SIL AFTER CONIZATION**

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**Objective:** To analyse if HPV determination is useful as a predictor factor of SIL persistence/relapse after conization.

**Method:** We analyzed a consecutive serie of 92 patients who underwent conization after HSIL diagnostic, between january 2001 and june 2004. The high risk HPV-DNA testing was done using PCR determination between 6 weeks and 6 months after treatment. Minimal follow-up period was 12 months, monitored by Pap smears and colposcopy. The results were correlated with other prognostic factors for recurrent HSIL, as CIN at cone margin or endocervix, high risk HPV, menopausal status.

**Results:** 17 cases of HSIL relapse were detected (18,5%). Whereas the PPV of HPV-DNA presence was low, only 2 patients with negative HPV-DNA recurred, then determination of HPV-DNA was more useful in predict the absence of a second lesion.

**Conclusions:** The use of HPV testing in the follow-up of treated HSIL, provides additional information about the risk of relapse in negative HPV-DNA cases. Just in positive cases for high risk HPV, it would be necessary an strict cytologic and colposcopic examination during follow-up after conization.

000165

**PREDICTIVE VALUE OF FOCAL ADHESION KINASE IN CERVICAL CANCER STAGE I AND II: A CLINICO-PATHOLOGIC STUDY**

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**Introduction:** Focal Adhesion Kinase (FAK) is a protein tyrosine kinase that is a critical mediator of signaling events between cells and their extracellular matrix. FAK is overexpressed in a variety of human solid tumors and its expression has been correlated with early tumor cell invasion and metastasis, but data on cervical cancer are inconclusive. We analyzed FAK protein expression and correlated these findings with patients survival.

**Materials and Methods:** In this retrospective study FAK protein was evaluated by immunohistochemistry in formalin-fixed paraffin-embedded tissue from 162 samples of cervical cancer, collected between 1988 and 1995. FAK expression was correlated with clinicopathological parameters to analyze its prognostic impact.

**Results:** The expresssion of FAK was confined to the cytoplasm and the cell membrane of the tumor cells. Normal epithelium showed barely any FAK expression. Of 162 cervical cancer samples, 55 (34%) showed weak expression of FAK, whereas moderate and high expression was found in 63 and 44 tumors (66%), respectively. Patients with tumors expressing weak amounts of FAK were characterized by a significantly poorer survival compared to those with moderate or high intratumoral FAK expression ($p = 0.007$, log rank test). Weak expression of FAK correlated with lymph node involvement ($p = 0.02$) and tumor recurrence ($p = 0.04$). Multivariate Cox regression analysis revealed that FAK expression was a significant independent predictor for survival.

**Conclusion:** The specific expression in tumor tissue indicates an important functional role of FAK in cervical cancer. The survival data strongly indicate that FAK protein expression in cervical cancer tissue is an independent prognostic factor.

000166

**AGGRESSIVE PLACENTAL SITE TROPHOBLASTIC TUMORS. REPORT OF TWO CASES**

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Placental site trophoblastic tumor (PSTT) is a rare trophoblastic lesion, derived from the implantation site intermediate trophoblast. We report two cases, occurring in young women of 25 and 33 years old. Clinically, the first patient presented vaginal discharge. An uterine resection was performed for a fibroma, showing, at histological examination, an infiltration of the myometrium by isolated enlarged cells, corresponding to a PSTT. The other patient went to hospital for a curettage after a spontaneous abortion and the diagnosis of PSTT was performed on the endometrial biospy. An uterine perforation at the time of curettage occurred. In both cases, HCG beta levels remains high, and MRI showed the presence of residual tumor. An hysterectomy was performed. On hysterectomy specimens, PSTT was still present, and infiltrated more than on half of the myometrial depth. The tumoral cells were positive for inhibin alpha, HPL, HCG beta, whereas ER and PR were negative. Some of the tumor cells were immunolabelled for p53. The proliferation index, assessed by the detection of Ki67 in both cases was at 10%, and areas of necrosis were present in the biopsies as well as in the surgical specimens. These criteria are linked to a more aggressive behavior of the tumor and the detection of p53 could play a role in the tumoral potential of the trophoblastic cells.

000167

**UNITED KINGDOM COLLABORATIVE TRIAL OF OVARIAN CANCER SCREENING (UKCTOCS): OUTCOME REVIEW PROCESS**

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UKCTOCS is a randomised control trial of ovarian cancer screening. 200,000 postmenopausal women aged 50 to 74 are randomised to ultrasound, serum CA125 or control in 1:1:2 ratio. The primary outcome is ovarian cancer mortality. The objective of this report is to describe the outcomes review process aimed at ensuring unbiased classification of ovarian cancer diagnoses and deaths. The coordinating centre is notified of all cancers and deaths through the Office of National Statistics via a 'flagging' study. In addition, information is obtained directly from collaborating centres and participants via postal questionnaire. An independent outcomes committee, consisting of epidemiologist (chair), gynaecological oncologist and pathologist, reviews all data (death certificates, ONS cancer registration; histology reports; operative notes and discharge summaries) on cancers and deaths with specified ICD codes. These are chosen to encompass all possible ovarian pathology and in addition to C56 (primary malignant ovarian neoplasm), include others like C76 (malignant neoplasm of abdomen and pelvis), C80 (malignant neoplasm without specification of site), D39.1 (neoplasm of uncertain behaviour of ovary) etc. The committee is blinded to the randomisation group. Outcomes are classified as definitely ovarian cancer or probable, possible or uncertain. Difficult cases identified by the outcomes committee will be reviewed by multidisciplinary input from independent gynaecological oncology experts. A pilot pathology review of slides is planned to evaluate the impact on final ovarian cancer diagnosis. It is inevitable that there will be better documentation for

screen-detected cancers. It is therefore essential that there is well-established protocol aimed at minimising bias.

000168

**THE ROLE OF CYCLIN-A, CYCLIN-E AND P-27 IN NORMAL ENDOMETRIUM AND ENDOMETRIAL PATHOLOGIES**

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**Objective:** To demonstrate the role of cyclins (Cyclin-A, Cyclin-E) that play role in cell proliferation cycle and the role of P27 gene that is known as tumour supressor gene in endometrial cancer, endometrial hyperplasia and proliferative endometrium by immunohistochemical methods.

**Material and Methods:** This study is carried out among 75 patients; in the first group there were 25 stage I endometrioid type endometrial cancer patients, in the second group there were 25 simple endometrial hyperplasia cases, and in the third group 25 proliferative endometrium cases were included.

**Results:** When groups were compared for Cyclin-E immunoreactivity; there were statistically significant differences between the first group and second group, the first and the third group ($P < 0.05$). When groups were compared for Cyclin-A immunoreactivity; no statistically significant differences were found among the groups ($P > 0.05$). When the groups were compared for P27 immunoreactivity; a statistically significant differences were detected among the groups ($P < 0.05$).

**Conclusion:** As a result, Cyclin-E was found probably to play role in the development of endometrial cancer. P27 was found to be effective at the progression of endometrial hyperplasia and endometrial cancer. It may be proposed that the histopathologic evaluation of Cyclin-E and P27 in patients with endometrial hyperplasia who were planned to be treated medically; these may be important for the evaluation of future development of the endometrial cancer.

000169

**ANTISENSE CHEMORADIOIMMUNOTHERAPY COMPOSED OF ANTICYCLIND1SCFV LINKED ONTO RADIOISOTOPES, VINORELBINE, PROCAINAMIDE & 21NUCLEOTIDE DOUBLE-STRANDED SIRNA TARGETED TO IRF9 INDUCE ANOIKIS & APOPTOSIS IN METASTATIC BREAST CANCER**

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Metastatic breast Ca is resistant to cytotoxic drugs and radiation making it one of the most aggressive malignancies. We obtained surgically 137 metastatic breast Ca specimens from patients. Genomic DNA of tumours was analysed for CpG island hypermethylation by using MS-PCR. All of the tumours showed hypermethylation of tumour suppressor genes with the following frequencies: E-cadherin 92%, p16 89%, RASSF1A 84%, RARb2 78%, hMLH1 60%, BRCA2 54% and p53 51%. IHC,WB,SB and RT-PCR exhibited overexpression of DNMT1, IRF9/p48/ISGF3g, cyclinD1, bcl-2, Raf1 and cdc25c. We treated the MBC with anticyclinD1scFv attached onto high energy radioisotopes, vinorelbine, procainamide and 21 nucleotide double stranded siRNA segment generated against IRF9. Post-treatment, we detected re-expression of tumour suppressor genes after inhibition of DNMT1 by demethylating procainamide. There was downregulation of cyclinD1 due to targeted scFv and inactivation of bcl-2, Raf1 and cdc25c due to phosphorylation by vinorelbine. We detected upregulation of p21Waf1, p27Kip, Bid and Bak. The 21nucleotide double stranded siRNA targeted to IRF9 inhibited its mRNA. The high energy radioisotopes induced DNA double strand breaks in MBC cells arresting synergistically with MT depolymerizing vinorelbine their growth at the G2/M transition according to flow cytometry analysis. We detected externalization of PS, depolarization of mitochondrial transmembrane potential, activation of caspase-3,7,8,9 and bax, cleavage of poly (ADP-ribose) polymerase and DNA fragmentation. TEM exhibited D2 apoptotic signs forming apoptotic bodies which were phagocytosed by adjacent tumour cells leading to an autophagocytic bystander killing effect associated with overexpression of typeII LC3. TEM exhibited signs of anoikis. BrdU and MTT exhibited inhibition of DNA synthesis and metabolic activity of treated MBC cells compared to untreated controls. We have achieved to eradicate MBC cells chemoresistant to taxanes with combined chemoradioimmunotherapy after circumvention of chemo and radioresistant mechanisms.

000170

**ANASTROZOLE, HYDRALAZINE AND VINORELBINE INDUCE APOPTOSIS IN BREAST INFILTRATING DUCTAL CA OF A POSTMENOPAUSAL PATIENT WITH HYPERMETHYLATION OF AROMATASE (CYP19) GENE AND ER**

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Postmenopausal women produce estrogens through the aromatase (CYP19) gene which is present in high concentrations in breast cancer or its stroma. Although breast Ca is sensitive to endocrine intervention in sequence, eventually resistance will occur. We obtain cancer cells from a resistant to treatment postmenopausal patient with advanced infiltrating or invasive ductal carcinoma (IDC). MSP detected coincident aberrant 5′CpG island hypermethylation of aromatase (CYP19) and ER which caused their transcriptional silencing. Loss of ER and CYP19 expression was associated with poor histological differentiation, high growth fraction and poor clinical outcome. PCR exhibited overexpression of antiapoptotic oncogene bcl-2 which causes chemoresistance. After combined administration with aromatase inhibitor with anastrozole, DNA methyltransferase inhibitor hydralazine and vinorelbine, we observed phosphorylation and downregulation of bcl-2, CpG island demethylation and re-expression of CYP19 and ER protein and inhibition of the metabolic transformation of androgenic precursors into estrogens. All these induced apoptosis in tumour cells according to TUNEL. TEM exhibited irreversible D2 apoptotic signs such as disintegration of tumour cells to membrane bound apoptotic small bodies which were phagocytosed by adjacent tumour cells leading to a bystander killing effect. Concluding, this therapeutic approach may revolutionize treatment against advanced breast infiltrating ductal carcinoma resistant to treatment due to potential advantages offered in comparison to conventional therapy such as well defined mode of action, selectivity and mainly circumvention of resistance to treatment by causing DNA demethylation reactivating transcriptionally silenced genes such as CYP19 and ER downregulating by phosphorylation antiapoptotic oncogene bcl-2.

000171

**CLINICAL OUTCOMES OF PRIMARY AND INTERVAL DEBULKING SURGERY IN ADVANCED OVARIAN CANCER**

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**Background:** Primary Debulking Surgery (PDS) followed by chemotherapy is still considered the optimal treatment for advanced Epithelial Ovarian Cancer. Unfortunately, it is associated with a high risk of morbidity and intraoperative complications. We examined the impact of Interval Debulking Surgery (IDS) on clinical outcomes of patients considered unsuitable for PDS (as optimal cytoreduction was not anticipated) and compared them with outcomes of women that had PDS followed by chemotherapy.
**Patients and Methods:** Non-randomised prospective study of 35 patients who underwent IDS and 29 patients treated with PDS. All patients had stage IIIC or IV disease and were treated by the same two surgeons. The IDS patients were considered unresectable based either on pre-operative CT or laparoscopy findings. All patients received the same regimen of chemotherapy.
**Results:** There was no significant difference regarding patients' age and tumour stage. Optimal cytoreduction rate was similar in both groups. The mean blood loss and the possibility of admission in the Intensive Treatment Unit (ITU) were significantly less in the IDS group. The risk of postoperative complications (chest, wound and urinary infection) and duration of hospitalization were also less in the IDS group but did not reach statistical significance.
**Conclusions:** IDS in patients with 'unresectable' disease seems to achieve similar rates of optimal debulking as PDS, with reduced need for blood transfusion and ITU care. In the absence of any evidence of adverse effects on progression free and overall survival, IDS could evolve as treatment of choice for selected patients with advanced ovarian cancer.

000172

## ENDOMETRIAL CANCERS IN WOMEN UNDER 40 YEARS: INSIGHTS FROM THE MCGILL EXPERIENCE

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**Objective:** To determine the optimum management of endometrial cancer (EC) in women below 40 years.
**Results:** 31 of the 1194 women with EC treated surgically at our institution between 1989 and 2003 were below 40 years. 58% were nulliparous. Although the preoperative assessment suggested low risk pathology in 93.5% of patients, the final pathology was high-risk in 19%. Positive lymph node metastases were found in 20% of the patients who had full surgical staging despite low-risk pathology. Of the patients who had a bilateral salphingo-oohorectomy despite the preoperative low-risk pathology, 13% had unexpected synchronous ovarian primaries and one had a fallopian tube metastasis. One patient with grade II endometrioid adenocarcinoma, who had not had full surgical staging, developed inguinal metastatic disease 15 months later. Assessment of sexual functioning or menopausal symptoms did not form part of the routine follow-up evaluation. Apart from the patient with recurrence in the inguinal nodes, one patient with Stage IV disease died at 13 months, one Stage I patient died of recurrent breast cancer. The remaining patients are alive and free of disease -median follow-up 69.86 months.
**Conclusion:** In our experience, dispensing with surgical staging or retaining the ovaries on account of the young age and low risk preoperative pathology is unsafe and counterproductive as it may necessitate the use or pelvic radiotherapy to reduce the risk of recurrent disease. Menopausal symptoms and sexual dysfunction induced by surgical castration and adjuvant treatment should be addressed during follow-up of these young women.

000173

## CONSERVATIVE TREATMENT FOR VIN-III WITH TOPICAL IMIQUIMOD CREAM 5%

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**Objective:** To evaluate the efficacy, tolerance and recurrence rate after self-treatment with Imiquimod 5% of patients presenting VIN-III.
**Material and Methods:** Between September 1999 et April 2004, 45 patients with biopsy-proven VIN-III were prospectively offered conservative treatment with imiquimod 5%, twice weekly. Patients were followed every 6 weeks, photographs were recorded. Epidemiologic factors linked to VIN-III, response to treatment, side effects and recurrence rate were recorded.
**Results:** Mean age was 45 years (23-74). Thirty-eight patients (85%) were smokers, 2 were immuno-suppressed. Twenty-two (52%) were referred with recurrent VIN-III. Multifocal, polymorphic and cutaneo-muquous lesions were obeserved in 71%, 50% and 57% of the cases, respectively. Thirty-eight women completed at least 8 weeks of treatment. Complete responses (CR) occured in 24 patients (56.4%), partial response (PR) of at least 50% in 18 others (38.4%). Failure to treatment were observed in 1 immuno-depressed woman. The mean treatment time was 15 weeks (5-28) and besides local irritation and burning, no serious side effects were noted. Median follow-up was 18 months (2-52). Among CR, after a median follow-up of 24 months, only one patient (2.3%) recurred. Among PR, 5 patients recurred after a median follow-up of 15 months.
**Conclusions:** Self-application of imiquimod 5% is efficious and safe for VIN-III treatment. It may replace (for CR) or reduce (for PR) the surgical extent of VIN-III resection or ablation. Longer follow-up is necessary to confirm the low recurrence rate that might be the most important advantage of this conservative treatment.

000174

## HYPOXIA-INDUCIBLE FACTOR-1α AND GLUT-1 EXPRESSION IN HYPERPLASIA AND ENDOMETRIAL CANCER

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**Introduction:** Hypoxia-inducible-factor-1α (HIF-1α) plays an essential role in the adaptive response to hypoxia. The activated HIF-1α pathway triggers biologic events that are associated with aggressive tumor behavior. Glut-1 is a HIF-1α regulated facilitative glucose transporter allowing hypoxic tumor cells distant from stromal blood vessels to survive through glycolysis. We analyzed HIF-1α and Glut-1 in an endometrial carcinogenesis model.
**Methods:** Paraffin-embedded clinical specimens from inactive endometrium (IE, N = 19), endometrial hyperplasia (EH, N = 23) and endometrioid carcinoma (EC, N = 33) were used. HIF-1α nuclear and Glut-1 membrane expression were identified immunohistochemically.
**Results:** HIF-1α was seen in 5/19 IE cases, always in a diffuse, non-necrosis related expression pattern. EH showed diffuse HIF-1α in 12/23 cases, one of these also showing a perinecrotic pattern. EC showed a diffuse HIF-1α pattern in 26/33 cases, 7 of which also had a perinecrotic pattern ($p = 0.00$ $\chi^2$-test), 2/33 showed an exclusively perinecrotic pattern. Mean percentages of HIF-1α positive cells in IE, EH and EC were respectively 0.6 (0-5)%, 4.7 (0-20)% and 25.7 (0-90)%. There was no membranous expression of Glut-1 in IE and EH in contrast to 30/32 (93.8%) of EC, always in a perinecrotic fashion. In EC, perinecrotic HIF-1α and Glut-1 were strongly correlated ($\chi^2$-test; $p = 0.00$).
**Conclusion:** HIF-1α shows increasing overexpression from IE through EH to EC, whereas perinecrotic, hypoxia associated HIF-1α

overexpression is absent in IE, rare in EH and frequent in EC. The association between perinecrotic HIF-1α and Glut-1 expression points to functional HIF-1α. We postulate that HIF-1α plays an important role in carcinogenesis of endometrial cancer.

000175

**MICROSATELLITE ALTERATION IN BENIGN, BORDERLINE AND MALIGNANT EPITHELIAL TUMORS OF THE OVARY**

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Some genetic alterations are involved in ovarian carcinogenesis. Since some benign and borderline tumors may represent early steps in ovarian carcinogenesis, analysis of precursor lesions could provide evidence that an accumulation of genetic events is required in order for normal ovarian epithelium to generate benign, borderline, malignant tumors. Few pre-invasive ovarian tumors have so far been studied. 60 cases of ovarian epithelial tumor, including benign, borderline, and malignant tumors, were analyzed for microsatellite instability (MSI) by gel analysis of paired germ line and tumor DNA. PCR amplification was performed using the panel of 5 microsatellite markers recommended by the NCI (BAT25, BAT26, D2S123, D5S346, D17S250) and 6 additional markers (D1S160, D1S162, D7S522, D11S860, D17S855, D17S932). In this study, D2S123 and D5S346 were the most frequently altered markers in malignant ovarian tumors and D11S860 locus showed MSI in 4 adenomas, 4 borderline tumors, and 12 malignant tumors. Other markers displayed instability with only one or two tumors showing MSI. On the basis of NCI criteria, most benign tumors demonstrated microsatellite stable (MSS). In the borderline tumors, 10 tumors revealed MSS, 8 tumors had low-frequency MSI (MSI-L), and two tumor had high frequency MSI (MSI-H). In the malignant tumors, 6 tumors revealed MSS, 2 tumor had MSI-L, and 12 tumors had high MSI-H. According to the result, MSL-H is more frequently seen in the malignant tumors. D2S123 and D5S346 were the most frequently altered markers in the malignant tumors, and D11S860 locus may be involved in the early step of carcinogenesis.

## *Poster Group 1B – Monday, September 26, 2005*

000176

**OVARIAN CANCERS: EPIDEMIOLOGY, MANAGEMENT AND PROGNOSIS. SHEFFIELD CASE SERIES OF 871 PATIENTS**

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**Objective:** To determine epidemiology, management and outcome of ovarian cancers managed in Sheffield.

**Methods:** Prospective case series of 871 patients.

**Results:** Age = 6-93 yrs, mean = 59. 34% had medical problems: Hypertension = 27%; Ischaemic heart disease = 16%; Diabetes = 6%. Speciality first referred to: Gynaecology = 45%; Surgery = 35%, Medicine = 12% and others = 8%. Symptoms: Abdominal distension = 43%, Pain = 37%, Bloatedness = 16%, Bowel disturbance = 10%, PMB = 9%, Mass = 3%, Urinary = 1.5% and others < 1%. 42% had > 1 symptom. Symptom duration = 0-48 months. Investigations: USS = 90%, CT = 34% and MRI = 5%. Ca125 levels raised (>35IU) in: All ovarian cancers = 85%, Epithelial ovarian cancers (EOC) = 89%, primary peritoneal tumours (PPT) = 100% and Borderline tumours = 60%. Surgery performed in 95%. Operation was: 1st = 85.6%; 2nd = 13.7% and 3rd = 0.7%. Procedure performed: BSO = 70%, hysterectomy = 68% of those with a uterus, Omentectomy = 68%, Appendectomy = 6%, small bowel resection = 2.5%, Large bowel resection = 5.7%, Omental biopsy = 1.7%, LSO = 6%, RSO = 9% and debulking = 8%. Incision: Vertical = 93%; Transverse = 7%. Ascites present = 61% and positive of malignant cells = 80%. If Ascites absent, washing taken in 93% & positive of malignant cells in 23%. Residual disease range = 0-20 cm: 0cm = 50%; 0-2cm = 27%; >2cm = 23%. Histology: Borderline = 16%; Epithelial = 74%; PPT = 3%; Germ cell = 1.2%; Sex cord stromal = 2%; Mixed mullerian = 0.5%; Non-epithelial = 1%; Metastatic = 2.5%. EOC type: Serous = 50%; Endometrioid = 20%; Mucinous = 11%; Clear cell = 8%; Serous papillary = 5%: Mixed pattern = 5%. FIGO staging for: All tumours: I = 30%, II = 9%, III = 51% & IV = 10%; Epithelial ovarian carcinomas I = 24%, II = 9.8%, III = 57% and IV = 9.8%. Chemotherapy: 1: In all tumours Adjuvant = 60% and Neoadjuvant = 3.3%. 2: EOC = 80%; 3: PPT = 95% 4: Germ cell = 56%. 5-year survival: All ovarian cancers = 41%; EOC = 38.5%; Borderline = 83%; PPT = 33%; Sex cord = 66%. EOC stage I = 80%, II = 77%, III = 24% and IV = 28%.

**Conclusions:** The study highlights the epidemiology, management and outcome of ovarian cancers

000177

**TRENDS IN THE EPIDEMIOLOGY, MANAGEMENT AND OUTCOMES OF VULVAR CANCERS**

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**Aim:** To assess trends in epidemiology, management and outcomes of vulvar cancers.

**Methods:** Analysis of 230 vulvar cancers managed between 1981 and 2002.

**Results:** 92% of patients were managed surgically. 6% had primary radiotherapy. Surgical management, epidemiology and outcomes in cases managed between 1981 and 2002 are shown in Table 1. Management has evolved from 'en block' radical vulvectomy (13%), to triple incision (TI) vulvectomy (28%) and then radical wide local excision (WLE) with inguino-femoral lymphadenectomy (24%), with no significant change in survival. This has resulted in a reduction in need for plastic reconstruction (from 40% to 4%), post-operative morbidity and hospital stay (from 40 to 21 days). Adjuvant radiotherapy was given in 12%. 5-year all cause survival for SCC was 57%. The mean age has increased from 59 to 72 and this may explain the small non-significant reduction in all 5-year survival. FIGO stage, tumour size, grade and lymph node status were prognostic factors. Age, symptoms, duration of symptoms, tumour histology, FIGO stage, adjacent skin histology, tumour site, number of nodes

Table 1:Comparison of vulvar cancers management, epidemiology and outcomes between 1981 and 2002

| Year of management (Number of cases) | | 1981-1985 (5) | 1986-1990 (13) | 1991-1995 (46) | 1996-2000 (99) | 2001-2002 (28) |
|---|---|---|---|---|---|---|
| Management 'En block' radical vulvectomy | | 80% | 77% | 30% | 0% | 0% |
| Triple incision vulvectomy | | 0% | 8% | 48% | 28% | 25% |
| Wide local excision (WLE) + inguino-femoral lymphadenectomy | | 0% | 0%) | 2% | 36% | 50% |
| WLE/Excision | | 20% | 15% | 20% | 35% | 25% |
| Age (years) | Mean | 59 | 59 | 66 | 67 | 72 |
| | Median | 60 | 66 | 71 | 69 | 74. |
| Medical Co-Morbidity | Hypertension | 0% | 22% | 40% | 33% | 46% |
| | Diabetes | 25% | 0% | 9% | 15% | 15% |
| | Ischaemic heart disease | 0% | 20% | 25% | 16% | 12% |
| FIGO Stage | I | 40% | 53% | 39% | 39% | 54% |
| | II | 20% | 31% | 21% | 32% | 18% |
| | III | 40% | 15% | 20% | 19% | 25% |
| | IV | 0% | 0% | 20% | 9%) | 0% |
| 5- year survival (%) | | 100% | 75% | 52% | 57% | - |
| Hospital stay (days) | Mean | 40 | 34 | 33 | 18 | 21 |
| | Median | 39 | 32 | 31 | 16 | 23 |
| Plastic reconstruction | | 40% | 9% | 35% | 9% | 4% |

harvested, hospital stay, recurrence rate, medical co-morbidity were consistent with previous reports.
**Conclusions:** Management has evolved towards less radical surgery with reduced morbidity and hospital stay. Epidemiology and outcomes are comparable to previous reports.

000178

**PREDICTORS OF INGUINO-FEMORAL LYMPH NODE METASTASES IN VULVAL SQUAMOUS CELL CARCINOMA. CAN CONTRALATERAL LYMHADENECTOMY BE OMMITTED IN TUMOURS WITH ≤5 MM DEPTH OF INVASION?**

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**Objective:** To assess risk of inguino-femoral lymph node metastases in vulval tumours with cellular differentiation, tumour size and depth of invasion as predictors of lymph node metastases.
**Methods:** Prospective analysis of 90 vulval squamous cell carcinomas managed by radical tumour excision and inguino-femoral lymphadenectomy, between 1981 and 2002.
**Results:** Proportion of patients with inguino-femoral lymph node metastases according to tumour size, tumour differentiation and depth of tumour invasion in squamous cell carcinoma of the vulva are shown in table 1. Risk of ipsilateral and contralateral lymph nodes metastases increases with increasing tumour size, increasing depth of tumour invasion and worsening cellular differentiation. Of significance (p = 0.05 Chi squared test), no contralateral lymph node metastases occurred in the 39 tumours with a depth of invasion of ≤5 mm, compared to the 17% contralateral lymph node metastases in tumours with depth of invasion >5 mm.
**Conclusions:** Tumour size, depth of invasion and cellular differentiation are related to risk of lymph node metastases. No contralateral lymph node metastases occurred when tumour depth of invasion was ≤5 mm. This suggests that contra-lateral lymphadenectomy may potentially be omitted in patients with tumour depth of invasion ≤5 mm but further work is needed to validate these findings.

Table 1: Risk of Ipsilateral and contralateral lymph node metastases with: Tumour size, depth of invasion and tumour differentiation

| | | Ipsilateral lymph node metastases | | Contralateral lymph node metastases | |
|---|---|---|---|---|---|
| | | % | Proportion | % | Proportion |
| Overall | | 33% | (30/90) | 11% | (10/89) |
| Tumour size (TNM classification) | T1 | 27% | (13/48) | 8% | (4/48) |
| | T2 | 44% | (15/34) | 12% | (4/34) |
| | T3 | 25% | (1/4) | 33% | (1/3) |
| Depth of invasion | <1mm | 0% | (0/1) | 0% | (0/1) |
| | 1-3mm | 14% | (3/21) | 0% | (0/21 |
| | 3.1-5mm | 42% | (7/17) | 0% | (0/17) |
| | >5mm | 28% | (5/18) | 17% | (3/18) |
| Tumour differentiation | Well | 17% | (8/48) | 2% | (1/48) |
| | Moderate | 50% | (12/24) | 21% | (5/24) |
| | Poor | 47% | (8/17) | 23% | (4/17) |

000179

**ANALYSIS OF THE OUTCOME OF PATIENTS REFERRED FOR COLPOSCOPY AFTER ONE SMEAR SHOWING MILD DYSKARYOSIS**

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**Objective:** To assess the outcome of patients referred for colposcopy after one smear showing mild dyskaryosis.
**Methods:** Retrospective analysis of patients referred for colposcopy after one mildly dyskaryotic smear with a follow up period of 48 months. These women have never had any previous abnormal smears.
**Settings:** Colposcopy clinic, King's College Hospital, London.
**Results:** We identified 101 patients who were seen in the colposcopy clinic following one mild dyskaryotic smear. At 6 month, 69 (69%) patients had repeat smears; 37 (37%) had a normal smear, 16 (16%) borderline, 11 (11%) had persistent mild dyskaryosis, 3 (3%) inadequate smear, and only 2 (2%) showed moderate dyskaryosis. Of the remaining 32, nine patients (9%) failed to attend and 23 (23%) had their smears performed after 6 months; of these, 16 (16%) were normal, 4 (4%) borderline, 2 mild and one was inadequate. Over the four year period, only 14 patients (14%) required treatment with loop cone biopsy. Histology confirmed CIN I in one case (1%), CIN II in 6 patients (6%), CIN III in 3 (3%) and no evidence of CIN in 4 (4%)
**Conclusion:** 53% of patients who presented with one smear showing mild dyskaryosis subsequently had a normal smear; high grade CIN occurred in only 9% of patients. The results are reassuring and reveal a lower prevalence of high grade CIN in such women than has been previously reported. Our results suggest that colposcopic referral may not be necessary after only one mildly dyskaryotic smear.

000180

**THE EXPRESSION OF KI-67, P53, ESTROGEN AND PROGESTERONE RECEPTORS AFFECTING SURVIVAL IN UTERINE LEIOMYOSARCOMAS. A CLINICOPATHOLOGIC STUDY**

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**Objectives:** To evaluate the level of expression of estrogen receptor (ER), progesterone receptor (PR), p53 and Ki-67 in patients with leiomyosarcoma and to investigate the effect of these and to identify the clinical parameters on prognosis.
**Materials and Methods:** Twenty-four patients operated for LMS of uterine origin between 1994 – 2003 at Istanbul Medical School, Department of Obstetrics and Gynecology and Division of Gynecologic Oncology constituted our study group. The effects of stage, grade, chemotherapy, radiotherapy, number of mitoses, presence of necrosis, Ki-67 and p53 expression, presence of estrogen and progesterone receptors on survival were evaluated.
**Results:** The mean follow-up period of patients is 30.42 ± 25.15 months. The mean overall survival for all LMS patients was estimated to be 48.4 ± 10.38 months. The cumulative survival ratio in the 33rd month was 33.08. Age, menopausal status, history of prior radiotherapy, number of mitoses had no statistically significant effect on overall survival in our study although stage had a significant effect. Finding of greater than 10% steroid receptor expression has a positive effect on survival ([ER p = 0.019; log rank = 5.49] and [PR p = 0.023; log rank = 5.14]). There was a survival advantage in patients with Ki-67 expression (p = 0.034; log rank = 4.49) below the median value.
**Conclusion:** Surgical staging is an important prognostic factor in LMS patients. Contrary to the current literature, our findings suggest that estrogen and progesterone receptor positivity greater than 10% may be associated with a better prognosis.

000181

**BRCA1/BRCA2 MUTATIONS IN PRIMARY OVARIAN CANCER PATIENTS**

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**Objective:** Individuals carrying inactivating germline mutations in the breast and ovarian cancer susceptibility gene BRCA1 and BRCA2 have an increased risk of developing cancer. Germline mutations of the two genes are transmitted in the autosomal dominant fachion and predispose carriers to the development of ovarian and/or breast cancer.

**Methods:** We have screened 176 women with primary ovarian cancer for mutations in BRCA1 (185delAG and 5382insC) and BRCA2 (6174delT) gene in using mutagenically separated PCR, single strand confirmation polymorphism (SSCP) analysis followed by sequencing of variant bands.

**Results:** Three germlime alterations were identified: A frameshift mutation (5382insC) was observed in two ovarian cancer patients with familial cancer history. A unique amino acid substitution in exon 20 (G1748S) was seen in two patients and a splice site variant (IVS20 + 5 A>T) was deteceted in a patient with ovarian cancer. Moreover, a complex alteration (IVS20 + 5 A>T and G1748S) was also noted in two patients. However, 185delAG and 6174delT mutations were not observed in ovarian cancer subjects.

**Conclusion:** Our preliminary results indicate that BRCA1 gene are involved in some ovarian cancer patients, both with and without a family history, demonstrating the importance of BRCA1/BRCA2 in the development of ovarian cancer patients in Turkish population.

000182

**CYP1A1 GENE POLYMORPHISM AND RISK OF GYNECOLOGIC MALIGNANCIES**

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CYP1A1 is involved in xenobiotic metabolism, classified as phase I cytochrome P-450 enzymes that converts environmental procarcinogens to reactive intermediates with carcinogenic effects. To determine distribution of the CYP1A1*3 polymorphism (in exon 7 of the gene), we assessed the association of CYP1A1 gene polymorphism in 117 patients with epithelial ovarian cancer, 59 patients with endometrial hyperplasia, 94 patients with endometrial cancer, 61 patients with cervical intraepithelial neoplasia (CIN), 85 patients with cervical cancer and 202 control subjects. The CYP1A1 Ile/Val genotype significantly increase the risk of patients with epithelial ovarian neoplasm (O.R:5.7, 95%CI: 3.34-9.76). There were significantly differences in the distribution of Val/Val genotype among all patients (O.R:5.85, 95%CI: 2.4-14.25). Among endometrial hyperplasia, the higher frequency of patients with Ile/Val and Val/Val genotype (O.R: 5.0, 95%CI: 2.6-9.5 and O.R: 4.25, 95%CI: 2.3-7.84), respectively. Furthermore, there was statistical significant increase in relative risk association with Ile/Val and any Val genotype between endometrial cancer patients and controls (O.R: 3.0, 95%CI: 1.74-5.28 and O.R: 2.54, 95%CI: 1.5-4.32), respectively. Among CIN patients, there were significantly differences in the distribution of Ile/Val and any Val genotype (O.R: 4.5, 95%CI: 2.41-8.43 and O.R: 3.7, 95%CI: 2.03-6.78). Moreover, there was significantly differences in the distribution of Ile/Val and any Val genotype among cervical cancer patients (O.R: 6.4, 95%CI: 3.6-11.4 and O.R: 5.65, 95%CI: 3.2-9.8). Our results indicate that CYP1A1 gene polymorphism should be considered as an important risk modifier in the development of gynecologic malignancies and might be used as a predictive marker for gynecological carcinogenesis.

000183

**USE OF GNRH FOR TREATMENT OF SERTOLI-LEYDING-CELL TUMER**

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**Object:** To evaluate the effect of GnRH on sertoli-leydig-cell tumor in a 45-year old woman. Design: Case report Setting: A university hospital Patient: A 45-year old woman exhibited persistent elevation of testosterone (>2ng/ml) four months after surgery for sertoil-leydig-cell tumor of the ovary that suggested the presence of some residual active tumor.

**Result:** The serum testosterone levels returned to normal limits after 3 dose of GnRh and all tumor evaluation were negative. The patient was alive and free of disease 30 months of the treatment with GnRh.

**Conclusion:** GnRH may be an alternative choice for treatment a persistent or recurrent hormone-producing tumor of ovary.

000184

**PERITONEAL TUBERCULOSIS MIMICKING ADVANCED OVARIAN CARCINOMA: A CASE REPORT**

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**Background:** Mycobacterium Tuberculosis is worldwide the most frekwent cause of tuberculosis. The disease affects mainly the lungs, but in one third of patients other organs are also affected. Tuberculous perotonitis is an uncommon manifestation of extra-pulmonary infection. This can mimic a malignant abdominal proces.

**Case:** A 62-year-old female patient presented with abdominal swelling, thoracal pain and general malaise. Transvaginal ultrasound revealed ascites with adhesions and an omental cake. CT scan showed extensive omental and mesenterial implants. A CA-125 level of 538 kU/L was noted. We performed a diagnostic laparoscopy: ovarian cancer with extensive metastatic disease was suspected. The pathology report described necrotic granulomatous nodules. Mycobacteria could not be demonstrated on direct preparations. A new laparoscopy was performed to take new peritoneal biopsies for culture. These were positive for Mycobacterium Tuberculosis, sensitive for all tuberculostatics. This resulted in the final diagnosis of tuberculous peritonitis. Culture of urine and sputae remained negative. Antituberculosis treatment was started. Radiologic and laparoscopic pictures of peritoneal tuberculosis will be presented.

**Conclusion:** Tuberculous peritonitis and peritoneal carcinomatosis might share a similar clinical presentation, radiologic findings and elevated tumormarker. The potential for tuberculous peritonitis needs to be taken into account, especially in immigrants from countries with a high prevalence of tuberculosis. Laparoscopy with biopsies is an effective and safe method to make the diagnosis and to test the sensitivity to the tuberculostatics.

000185

**LYMPHOBLASTIC LYMPHOMA PRESENTING AS BILATERAL GIGANTOMASTIA IN PREGNANCY**

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Gigantomastia is a rare condition of excessive and generalized enlargement of the breasts, presenting in puberty and pregnancy. In most cases it is related to a benign cause, associated with an excess of circulating hormones or a target-organ hypersensitivity of mammary tissue to normal hormone stimulation. We present a case of bilateral gigantomastia in pregnancy as the primary presentation of a T-cell lymphoblastic lymphoma. Case report. A 29-year-old woman presented with extreme enlargement of the breasts at 30 weeks of twin-gestation. An excessive physiologic stimulation was hypothesised and a caesarean section was performed at 33 weeks because of preterm labor. After delivery magnetic resonance imaging of the breasts and thorax revealed bilaterally nodulated breasts and a 10 cm diameter mass in the anterior mediastinum. Biopsy of the mediastinal mass and the breasts revealed a T-lymphoblastic lymphoma. Treatment with multi-drug chemotherapy (according to the GMALL 93 protocol) was initiated and after 9 months the disease is in complete remission. Comment. Non Hodgkin's lymphoma presenting as bilateral gigantomastia during pregnancy is very rare. A literature search only revealed two reports where gigantomastia during pregnancy was due to a lymphoma. Pregnancy is likely to delay the diagnosis of malignancy that provokes gigantomastia, probably resulting in a higher stage and poor prognosis. Gigantomastia occuring during pregnancy therefore should alarm the clinician.

000186

**ENDOMETRIAL STROMAL SARCOMA COMPLICATING A 24 WEEKS TWIN PREGNANCY**

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**Objective:** A case of Uterine Endometrial Stromal Sarcoma diagnosed in pregnancy, which was initially diagnosed as leiomyoma is presented. This is the first reported case of midtrimester twin pregnancy-IVF with egg & sperm donation induced, in a 49-years-old woman.
**Case:** A 49-year-old single woman G2P0 post IVF with a presumed uterine subserous leiomyoma, was hospitalized on several occasions for vaginal bleeding that was first noted in the 13-th week of twin pregnancy. Serial ultrasound examinations revealed a fastly growing mass on the right side of the uterine fundus. She also developed a severe leukemoid reaction with WBC counts rising from 22,000/ml to 160,000/ml. She delivered spontaneously at the 24-th week 2 premature newborns. Several hours later she developed hemorrhagic shock due to intraabdominal bleeding. On emergency laparotomy a ruptured malignant mass originating in the uterine fundus with massive intraabdominal spread was discovered. Total abdominal hysterectomy,bilateral salpingooophorectomy and resection of transverse colon with end to end anastomosis were performed. The pathologic diagnosis was: Low and high grade endometrial stromal sarcoma. She died three weeks after delivery, and none of the newborns survived.
**Conclusion:** A strong desire to bear children should be carefully assessed in old women. Special attention should always be paid to rapidly growing uterine masses during pregnancy.

000187

**LAPAROSCOPIC BIOPSY VERSUS IMAGE GUIDED BIOPSY IN DIAGNOSIS OF SUSPECTED OVARIAN CANCER**

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**Background:** Laparoscopic and image guided biopsy techniques have been used for a long time but to our knowledge have never been evaluated or compared in the management of ovarian cancer.
**Aims:** To compare laparoscopic with image guided biopsies for diagnosis of suspected ovarian cancer with respect to accuracy, safety and guiding patient management. Materials and Methods: A retrospective case note study was performed for all biopsies taken for suspected ovarian cancer over 4 years from 31/6/2000 to 1/7/2004.
**Results:** 47 image guided biopsies (Group I) and 41 laparoscopic biopsies (Group II) were evaluated. The mean age in years was 68.2 in groupI and 60.3 in group II. WHO performance status was >2 in 35 of group I and 7 of group II patients. Tissue sample was inadequate in 3 group I cases, while all group II samples were adequate. There were no complications in group I but group II had 1 port site haematoma, 1uterine perforation and 1 anaesthetic complication. There were 4 inconclusive and 2 false negative reports in group I. Group II had 3 false negative reports. Overall procedure cost for group I was £290 and £ 2101 for gp II. Cases in groupI were older ($p < 0.01$) and had a poorer performance status as compared to group II ($p < 0.001$) but adequate tissue biopsy ($p = ns$) was obtained with no complications ($p = ns$). Cost ratio was 1:7.2. Both modalities were found equally useful in guiding patient management.
**Conclusion:** Image guided biopsy is an accurate, safe and a cost effective alternative to laparoscopic biopsy in medically compromised cases of ovarian cancer.

000188

**DETERMINANT FACTORS FOR OMENTAL METASTASES IN ENDOMETRIAL CANCER**

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**Objective:** To evaluate the factors in endometrial cancer which may predict the endometrial spread of the disease to omental tissue
**Material and Methods:** Data of 47 endometrial cancer patients have been retrospectively reviewed and analyzed.
**Results:** Twenty-nine omentum sampled and 18 not sampled endometrial cancer patients (n = 47, mean age: $62,7 \pm 9,8$) were investigated for omental specimen positivity (3,4%), recurrence (2,1% in median follow-up of 12 months), lymphovascular space invasion (LVSI, 20% positive), stage of disease (72,3% stage I), grade of disease (57,5% grade I, 25,5% grade II and 17% grade III), histologic type (85,1% endometrioid type adenocarcinoma), CA-125 level (<35 IU/ml in 85,4%) and adjuvant therapy (36,2% only followed, 53,2% given radiotherapy and 10,6% had chemotherapy). There was no significant difference in terms of recurrence in omentum sampled and not sampled patients ($p > 0,05$). In omental specimen available subjects there was no statistically significant difference found for LVSI ($p = 0,18$, OR = 1,25 95% CI: 0,8-1,9), age ($p = 0,62$) and number of lymph nodes sampled ($p = 0,35$) but statistically significant difference was detected for CA-125 ($p < 0,001$), stage ($p = 0,034$) and histologic type ($p = 0,001$) for omental specimen positivity.
**Conclusion:** Eventhough the spread, type and agressivity of tumor seems to be positively correlated with the omental positivity in the endometrial cancer patients, our results suggest that none of these factors are reliable to determine the state of omental metastasis. Omentectomy should still be a part of endometrial cancer surgery since these predeterminant factors are weakly associated with the decision that it should be abondoned.

000189

**DETECTION OF HUMAN PAPILLOMAVIRUSES IN OVARIAN MALIGNANCY BY POLYMERASE CHAIN REACTION**

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**Objective:** The role of HPV infection in ovarian cancer is unclear. The aim of this study was to investigate association between HPV and epithelial ovarian cancer.
**Materials and Methods:** The patients group consisted of 67 epithelial ovarian carcinomas (52 serous adenocarcinomas, 15 mucinous adenocarcinomas). The control group - of 25 nonmalignant ovarian tissues collected from women with uterine pathology undergoing pelvic surgery. DNA was isolated from snap-frozen ovarian tumor tissues and polymerase chain reaction (PCR) kits were used to detect the presence of HPV in tumor DNA samples.
**Results:** HPV DNA was detected in 76% of tumor samples. Only 8% of normal ovarian tissue samples were positive determined by PCR ($p < 0{,}001$). There was no correlation between HPV infection and histological type of ovarian cancer. The positive rate is 75% of serous adenocarcinomas and 80% mucinous adenocarcinomas ($p > 0{,}05$). Among samples of epithelial ovarian carcinomas more frequently were revealed HPV-18-30%, 52-30%, 55-27%, 83-18%, 39-16% types. HPV-18 type was significantly higher in mucinous adenocarcinomas (80%) compared to serous cancer (15%) ($p < 0{,}001$); HPV-52 (36,5%), 55 (32,7%) types - in serous adenocarcinomas compared to mucinous cancer (7% and 7% respectively) ($p < 0{,}01$).
**Conclusions:** Our results support an association between HPV-18, 52, 55, 83 and 39 types and epithelial ovarian malignancy. The prevalence of HPV infection in ovarian cancer is much higher than normal ovarian tissues, suggesting that HPV may play a role in the development of ovarian cancer.

000190

**DETECTION OF HUMAN PAPILLOMAVIRUS DNA IN OVARIAN CARCINOMA**

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**Objective:** The aim of this study was to examine the presence of human papillomavirus (HPV) DNA and genotyping in ovarian carcinomas.
**Materials and Methods:** The presence of HPV DNA in 100 cases of primary ovarian cancers was detected in paraffin embedded samples by polymerase chain reaction (PCR). PCR amplifications were done by MY09/11 primer set after digestion and phenol-chloroform extraction of the DNA. HPV PCR positive samples were analyzed and genotyped by OpenGene automated DNA sequencing system (Visible Genetics, Canada).
**Results:** HPV DNA was detected in 9 (9%) samples. HPV-16 DNA sequences were identified in 7 (7%) while HPV-33 were found in 2 (2%) of the 100 studied ovarian carcinoma samples. Histology of the 7 HPV-16 positive cases showed that there were 1 granulosa cell tumor, 6 serous papillary cystadenocarcinoma. HPV-33 were found positive in 2 (2%) of the studied samples. Histology of the 2 HPV-33 positive cases were serous papillary cystadenocarcinoma. No other HPV types were detected in the tested samples. So, in HPV positive cases the histologic dominance was 8 (88,8%) serous papillary. In studied cervical samples 2 of 5 cases were found positive, in one HPV 16 and the other case was HPV 33 positive, while in ovarian tissue of these two cases HPV 33 positivity was detected.
**Conclusion:** The HPV posititivity is well known etiologic factor in cervical cancer, but it is role in ovarian cancer pathogenesis is not clear with 8% positivity, and if present may plays a minor role.

000191

**RADICAL PARAMETRECTOMY IN THE TREATMENT OF INVASIVE CERVICAL CANCER AFTER SIMPLE HYSTERECTOMY**

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**Objective:** To assess the morbidity and efficacy of Radical Parametrectomy (RP) performed following simple hysterectomy in patients with invasive cervical carcinoma.
**Methods:** Seven year retrospective chart review identified 5 patients that underwent RP with pelvic and paraaortic lymphadenectomy and upper vaginectomy. Data were collected on demographics, tumor stage, histology and survival.
**Result:** One patient had stage IA lesion, one stage IB1, 2 patients had stage IIA, and one with unknown stage. One of these patients had adenocarcinoma. Median age was 41.6 years. The most indication for hysterectomy was abnormal vaginal bleeding (3 out of 5, 60%). Two patients had pelvic node metastases. Surgical margins in all 5 patients were tumor free at the time of RP. Two patients with positive pelvic nodes received adjuvant radiotherapy. Mean follow up time was 48.8 months. Four patients are alive without disease, and one patient who had been node positive, died 12 months after receiving radiation.
**Conclusion:** RP is an acceptable option for patients diagnosed with incidental finding of invasive cervical cancer at the time of simple hysterectomy. Careful selection of RP for patients not having residual tumor, will obviate adjuvant radiotherapy in most cases.

000192

**CANCER OF THE VAGINA AT THE LOWER THIRD TREATED WITH WIDE LOCAL EXCISION, MODIFIED MARTIUS FLAP INTERPOSITION AND BILATERAL INGUINAL-PELVIC LYMPHADENECTOMY**

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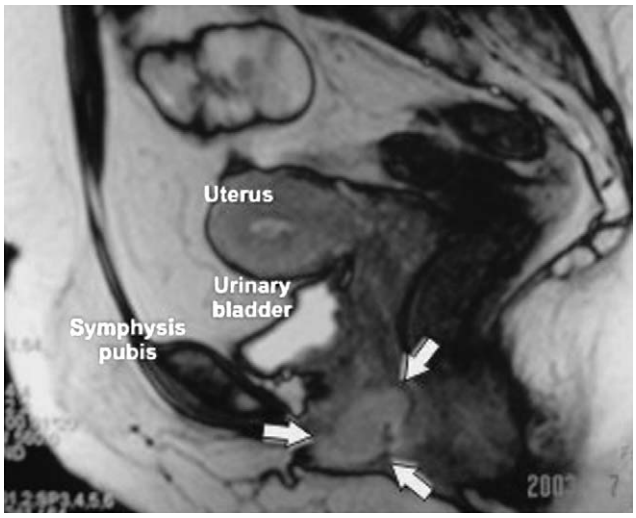
**Background:** Vaginal cancer is uncommon and occurring in less than 2% of the patients with gynecologic malignancies. And approximately 30% of the vaginal carcinoma lesions occur in the lower third of the anterior wall
**Case:** Sixty-four year old woman admitted with postmenopausal bleeding; during pelvic examination suburethral ulcerative 4x3cm mass was detected. The magnetic resonance imaging of the pelvis revealed mass lesion on the anterior wall of the vagina that is not discernible from the urethra. Biopsy result of the suburethral mass was squamous cell carcinoma. Mass was excised till negative borders are obtained, due to this external 3rd of urethra was also resected. And modified Martius flap interposition was added to the surgical procedure to support urethra. Inguinal and pelvic lymphadenectomy revealed 2 cm left inguinal and 1,5 cm right obturator lymphadenopathy, and obturator lymph node was metastatic. Post-operative adjuvant radiotherapy was also given.
**Conclusion:** Martius flap interposition is one of the surgical procedures that tend to be forgotten. In homology with use of forceps the state of art in surgery should not be left to the books on the dusty shelves of the library in gynecologic oncology.




000193

**DNA PLOIDY ANALYSIS AND THINPREP CYTOLOGY ARE METHODS OF COMBINED CORRELATION OF THE FINAL DIAGNOSIS IN A CASE OF EPITHELIAL OVARIAN CANCER**

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**Objective:** The aim of our study is combined correlation of the final diagnosis with DNA ploidy and ThinPrep method and amelioration of the diagnostic accuracy in a case of malignant epithelial ovarian tumors.
**Methods:** Our study was carried out on 105 patients with malignant epithelial tumors of the ovary. The age of our patients ranged from 22 to 70 years. (Mean value 45.2, SD = 18, 35). For ThinPrep cytology two smears (1 stained by Papanikolaou and 1 by Feulgen) were prepared. In the Feulgan stained smears DNA ploidy measurements were performed using SAMBA 2004 image analyzer.
**Results:** The 60, 95% of the cases of our materials were aneuploid and the remaining 39, 04% euploid. The results detect diploid DNA in 20 from 84 cases of IIC-IV stage (23, 80%). In 4 cases with false negative cytological results aneuploid DNA was detected in the histogram of static cytometry. A statistically significant difference was observed between the final cytological diagnosis and the ploidy status for discrimination of malignant from mesothelial cell ($x2 = 11$, 25, $p < 0{,}001$). The sensitivity, specificity, predictive value of positive result, predictive value of negative result and the diagnostic accuracy of the final cytological diagnosis and DNA ploidy analysis were 97,62%, 100%,100%,91,3% and 98,09% respectively
**Conclusion:** DNA ploidy can not be use as independent diagnostic criteria and only combined DNA ploidy analysis and ThinPrep methods show effective increase of diagnostic accuracy, can be use for the final diagnosis correlation and determinate of prognosis.

000194

**RADICAL VAGINAL TRACHELECTOMY AND LAPAROSCOPICALLY PELVIC LYMPHADENECTOMY FOR PRESERVATION OF FERTILITY IN EARLY CERVICAL CARCINOMA - A CASE REPORT**

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**Objective:** Radical trachelectomy was developed by Dargent as an alternative surgical treatment for cervical cancer. The techique was performed by laparoscopic approach and vaginal route, in the same way as vaginal radical hysterectomy, but the cervix is removed, only.
**Case report:** A 32 year old woman presented microinvasive carcinoma of the cervix after conization without patologic free margines. The patient desire fertility-sparing menagement. A radical trachelectomy was performed using the laparoscopico-vaginal approach. The procedure started with laparoscopic pelvic transperitoneal lymphadenectomy, the radical trachelectomy was carried by the quantity of suctioned fluids and weighed sponges. Operative time was measured from the time of troacar instillation to closure of the vaginal skin. Bladder function was assessed objectively after 3 dt day removal of the urinary catheter by performing ultrasound postvoiding residual urine. The patient was carefully followed up 1, 3, 6, 12 months with clinical examination, pap smear and routine ultrasound assessment. As complete clinical, cytological, ultrasound remission was confirmed to one year after surgical procedure, we accepted that the patient try to become pregnant.
**Discussion:** In early stage cervical carcinoma, the most important prognostic factors are tumor size and presence of lympho-vascular spaces invasion. When tumors are small and there is no invasion of the lymphatic space, the likelihood of lymph node involvement of later recurrence of carcinoma is low. In young women with cervical cancer with low risk factors for recurrence, preservation of fertility become an option.

000195

**A STUDY ON THE EXPRESSION OF P16 GENE, METHYLATION OF P16 GENE PROMOTOR AND HPV TYPING IN UTERINE CERVICAL NEOPLASIA**

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In cervical carcinogenesis, abnormality of p16 gene such as methylation of p16 gene promotor was investigated as an important factor like HPV (human papilloma virus). The aims of our study are to investigate the expression of p16 gene, methylation of p16 gene promotor, and HPV typing in uterine cervical neoplasia and to evaluate relationship between them in uterine cervical carcinogenesis. We investigated the expression of p16 gene with immunohistochemical method, methylation of p16 gene promotor with methylation specific polymerase chain reaction (MSP) and HPV typing with HPV DNA microarray. A total of 140 samples(-normal 10, CIN1, 31 CIN2, 3 62, invasive cancer, 37) were included. All cases were divided into two groups according to HPV DNA test.
**Result:** 1. In positive HPV group, P16 gene expression was observed in CIN1 (30.8%), CIN 2,3 (60%) and in invasive cancer (81%), p16 immunoreactivity was increased during carcinogenesis and there was increasing tendency of p16 gene expression in positive HPV group 2. Methylation of p16 gene promotor tended to be more frequent in negative HPV group especially during carcinogenesis.
**Conclusion:** 1. p16 gene expression that tended to be more frequent in positive HPV cases appears to reflect HPV induced cell cycle dysregulation 2. Methylation of p16 gene promotor may be one of the important mechanism for uterine cervical carcinogenesis especially in negative HPV cases. 3 The expression and promotor methylation of p16 gene may be molecular marker for early detection of uterine cervical cancer.

000196

**EIF-4E EXPRESSION IN THE PROGRESSION OF CERVICAL NEOPLASIA**

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eIF4E controls the translation of various malignancy-associated mRNAs which are involved in polyamine synthesis, cell cycle progression, activation of proto-oncogenes, angiogenesis, autocrine growth stimulation, cell survival, invasion and communication with the extracellular environment. We investigated whether the expression of eIF-4E is associated with the progression of cervical neoplasia. The eIF-4E expression was evaluated by immunohistochemistry in 89 formalin-fixed paraffin-embedded cervical tissues: 10 normal cervical specimens, 19 low-grade squamous intraepithelial lesions (LSILs), 20 high-grade squamous intraepithelial lesions (HSILs), and 40 invasive squamous cell carcinomas (ISCCs). The expression of eIF-4E was undetectable in normal cervical squamous epithelium, but had variable staining in the basal layer of normal endocervical glands. The expression gradually increased in accordance with the progression from LSIL to HSIL and ISCC ($P < 0.001$) and was detected in all cases of HSIL and ISCC. These results suggest that eIF-4E may play a significant role in tumor progression of cervical neoplasia and may represent useful markers for malignant transformation of cervical squamous cells. Further studies would likely result in the development of novel approaches for early detection and therapy for this disease.

000197

**THE ANTI-IDIOTYPIC MONOCLONAL ANTIBODY ACA125 IN PATIENTS WITH RECURRENT EPITHELIAL OVARIAN, FALLOPIAN TUBE OR PERITONEAL CANCER. A PHASE II TRIAL OF THE AGO-OVAR**

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**Background:** The majority of patients with advanced ovarian cancer will recur despite platinum-taxane first line therapy. ACA125 is a murine anti-idiotypic antibody of the tumor-associated antigen CA-125 and can lead to the generation of anti-anti-idiotypic antibodies (Ab3).

**Methods:** This multicenter phase I/II trial included 36 pts. with recurrent OC comparing two vaccination schedules: 9 (group A) vs. 6 injections (group B), 18 pts. in each group. Four sc injections at 2.0 mg were administered every two weeks and then monthly for 2 or 5 additional doses. Primary objective was safety, secondary objective immunological response.

**Results:** Treatment was completed as planned in 8 (44%) and 16 (89%) pts. in group A/B. No treatment limiting toxicities occurred in either group. The most common toxicity related to the vaccine was Grade 1/2 local injection site reaction. Other toxicities seemed to be related to the pts. disease and/or the prior chemotherapy. Induction of Ab3 was observed in all pts. except in two (A) and one (B) pts. who progressed prior to Ab3 evaluation (median titer 6 weeks after last vaccination, group A vs B: 359.6 μg/ml (range: 98.9-988.7) vs 209.6 μg/ml (range: 8.6-618.9), p = 0.0556). Both schedules showed no differences with regard to induction of HAMA (median titer 6 weeks after last vaccination, group A vs B: 8.1 μg/ml (range: 1.4-184.9) vs. 2.0 μg/ml (range: 0.017-13.2), p = 0.100) and IFN-γ secretion.

**Conclusions:** ACA125 vaccination is safe, well tolerated and induced humoral and cellular immune response. Both schedules were not different with regard to toxicity and immunogenicity.

000198

**TOWARDS UNDERSTANDING LOW LIBIDO IN CERVICAL CANCER SURVIVORS**

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The effects of radiotherapy and chemoradiation on hormone levels, with special regard to testosterone, and its effects on libido and sexual function in women with cervical cancer is by and large unknown. Sexual dysfunction, decreased sexual arousability, dyspareunia and low libido is well documented in cervical cancer survivors. In women oophorectomized for benign conditions, sexual dysfunction has been documented, and attributed to low testosterone levels. Treatment with testosterone in women (without cancer) with sexual arousal disorders often results in increased libido. No similar studies have been done on women with cancer, because of unknown or unwanted effects with regard to cancer. We are performing a pilot study on hormone levels after different kinds of treatment for cervical cancer. Our results will be correlated to the women's own reports of sexual function. The results are being collected, and the results will be presented at the conference.

000199

**LYMPH NODES INVOLVEMENT AND SURGICAL STRATEGY IN PATIENTS WITH ADVANCED OVARIAN CANCER**

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**Objective:** Aim of the study was to establish pelvic and paraaortic lymph nodes involvement and surgical strategy in patients with advanced ovarian cancer.

**Methods.** In this study we included 35 patients with ovarian cancer stage III and IV in whom total lymphadenectomy or lymph nodes resection was added to the standard surgery (panhysterectomy with omentectomy).

**Results.** Total lymphadenectomy was performed in 24 (68,6%) patients. 14 (58,3%) patients had clinically involved lymph nodes and in 10 (41,7%) cases lymphadenectomy was prophylactic procedure. Metastasis were found in 41,7% (10 patients). Lymph nodes resection was performed in 11 (31,4%) patients and in all cases there were clinical signs of their tumor involvement. Metastasis were found in 90,9% (10 patients) that was statistically significantly higher then in patients with total lymphadenectomy (p = 0,04). Resection of intraoperatively enlarged lymph nodes allowed us to predict their metastatic involvement in 84% cases. Prophylactic lymphadenectomy revealed metastasis in 25% of cases. Lymph nodes metastasis were found in 57,1% (20 patients). Pelvic lymph nodes were involved most often - in 31% of cases, paraaortic - in 11,4%, inguinal - in 8,6% and pelvic-paraaortic - in 5,7% of cases.

**Conclusion.** Metastatic lymph nodes involvement was found in 57,1% of patients with advanced ovarian cancer, mostly - in pelvic lymph nodes. Pelvic-paraaortic lymphadenectomy is indicated in case of clinical and/or intraoperative signs of lymph nodes involvement.

000200

**LYSOPHOSPHATIDIC ACID AS A TUMOR MARKER IN THE FOLLOW UP OF PATIENTS WITH EPITHELIAL OVARIAN CANCER**

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**Objective:** The aim of this study is to detect the plasma levels of Lysophosphatidic Acid (LPA) in epithelial ovarian carcinoma patients and to demonstrate whether it is usefull in the follow up of the disease as a tumor marker.

**Materials and Methods:** 29 epithelial ovarian cancer patients who were planed to receive chemotheraphy were included into the study. Patients recieved 6 doses of chemotheraphy with Paclitaxel + Carboplatin. Serum CA 125 levels were measured initially and before each chemotheraphy administration. Plasma samples of initial and before every chemotherapy administration were also collected and stored at - 80 C in deep freezer for LPA analysis. Gas chromotographic method was used for plasma LPA detection. LPA levels which were below the level of detection were assumed to be 0,1 mmol/L for statistical analysis.

**Results:** The mean preoperative plasma LPA level was 7.21±6.63 mmol/L. The same value was 5.21±5.32 mmol/L before the sixth chemotherapy. While means of plasma LPA values were not different from each other (p = 0,832)., medians of serum CA 125 were significantly different (p = 0,000) which were determined before each chemotherapy administration. Plasma LPA levels decreased slightly with chemotherapy administration and there was a weak negative correlation. (Spearman, rs = -0.151, p = 0.034). However, serum CA125 values declined with chemotherapy administration and there was a significant good negative correlation (Spearman rs = -0,596 p = 0,000).

**Conclusions:** In the follow-up of epithelial ovarian cancer patients that requiried adjuvant chemotherapy, measurement of plasma LPA levels have no superiority to the serum CA-125 levels.

000201

**THE ANALYSIS OF THE TREATMENT OF OVARIAN CANCER PATIENTS WITH NEO-ADJUVANT CHEMOTHERAPY**

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**Introduction:** Primary surgery and adjuvant chemotherapy is the standard treatment in ovarian cancer patients. Neo-adjuvant chemotherapy is one of the treatment modes in patients with poor general condition or advanced disease, not adjustable for primary surgery. The purpose of this study was to evaluate if the efficacy of this new option of therapy is comparable to the standard method.

**Materials and Methods:** 319 ovarian cancer patients, FIGO stage III and IV, have been analyzed. Within this group, 50 women were treated with neo-adjuvant chemotherapy. 18 patients were operated after 3 cycles of neo-adjuvant chemotherapy, and 32 patients - after 6 cycles. Results of treatment were evaluated, including disease free survival, and number of complications. Factors that may influence the treatment results were also analyzed.

**Results:** The median of disease free survival in the group treated with adjuvant chemotherapy (group 3), and operated after 3 cycles of neo-adjuvant chemotherapy (group 1), were 19 and 20 months, respectively. For the group operated on after 6 cycles of neo-adjuvant chemotherapy (group 2), the median of disease free survival was 15 months (p = 0,27). The following factors have been found to influence the treatment results: optimal cytoreduction and tumor grading. There was no difference in complications rate between three analyzed groups.

000202

**GENE EXPRESSION PROFILING IN EARLY STAGE CERVICAL CANCER**

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**Introduction and Methods:** Specific alterations in gene expression patterns might be used for molecular classification, prediction of disease outcome and treatment response. We determined the gene expression profile in tumours of 28 patients with early stage cervical cancer with (P) and without (N) lymph node metastasis after radical hysterectomy, using whole human genome oligonucleotide microarrays.

**Results:** We used an ANOVA based approach with multiple testing correction to identify signatures of gene expression. A group of 15 differentially expressed genes between the two groups was found, including genes that have been related in the literature to tumour growth and metastasis. Using a classifier, with 1000 random splits of the data in a training set of 20 patients (11N/9P) and a test set of 8 patients (4N/4P), the mean error rate was 36% with a 0-62 95% CI. Varying the training set size showed that the proportion of misclassification decreased as the training set size increased.

**Conclusion:** We found a possible signature of differentially expressed genes in patients with early stage cervical cancer with and without lymph node metastases. Our limited group size probably accounts for the 36% the misclassification rate, but a decreasing trend is seen when increasing the training set size. More samples are necessary to build a significant model.

000203

**THE ACTIVITY OF ENZYMES OF ESTROGEN METABOLIC PATHWAY: RELATION WITH STAGE, GRADE AND HISTOLOGICAL SUBTYPE**

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The purpose of the study is to reveal the correlation between the activity of estrogen metabolic enzymes in malignant endometrial tumors and Stage, histological subtype and differentiation Grade. A total of 57 patients with Stage 'in situ', I and II endometrial cancer were enrolled into the investigation. Activity of aromatase, catechol-O-methyltransferase (COMT), glutathione -S-transferase (GST) and total activity of 2- and 4-hydroxylases were assessed by radioenzymatic and spectrophotometric techniques. Variations in activity of estrogen hydroxylases, COMT and GST were found to be dependent on disease Stage and tumor depth invasion into the myometrium. The dependence of COMT activity on tumor Grade was also revealed. The COMT activity in well-differentiated endometrial cancers was significantly lower compared to that of moderately differentiated endometrial cancers. The relation of the activity of enzymes of estrogen metabolic pathway with the tumor histological subtype was found. The total activity of estrogen 2- and 4-hydroxylases in non-endometrioid endometrial tumors was higher compared

to that in endometrioid endometrial tumors. The detected correlation between the activity of enzymes of estrogen metabolic pathway and Stage and tumor depth invasion indicates that estrogen 2/4-hydroxylases, COMT and GST play an important role in tumor invasion and growth. The dependence of the activity of enzymes of estrogen metabolic pathway in endometrial cancers on histological subtype and differentiation Grade is under discussion.

000204

**RESULTS OF ADJUVANT BRACHYTHERAPY OF STAGE IB ENDOMETRIAL CARCINOMA**

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**Objectives:** We aimed to evaluate the pelvic control and survival rates with only high-dose rate brachytherapy in patients with stage IB endometrial carcinoma according to FIGO staging system.
**Materials and Methods:** We evaluated 54 patients retrospectively. The mean age of the patients were 60. All of the patients were stage IB. The grades of the 3 patients were unknown, 23 patients were grade 1, 27 of them were grade 2: and one of them was grade 3. The operational procedures were total abdominal hysterectomy + bilateral salpingo-oophorectomy for 29 of the patients and TAH+BSO+ lymphadenectomy in 25 of them. As adjuvant therapy, these patients had intracavitary treatment by double ovoids and using Curietron afterloading apparatus. The mean brachytherapy applied was 30 Gy.
**Results:** During the follow-up period no adverse event was seen in 33 patients, 14 of the patients had incontinence and 7 had proctitis. The mean follow-up period was 17 months. Pelvic control was achieved in 51 of the patients. Approximately 16 months following the end of the treatment 3 patients had pelvic recurrence. The local control rate was found to be 94.4%. One of these patients had distant metastasis 24 months after the treatment. One of the patients was dead at the 34th month of the follow-up period due to the disease and 3 of them were dead because of other reasons. General survival rate was 92.5%.
**Conclusion:** Brachytherapy alone as adjuvant therapy is sufficient for local control and survival in Stage IB endometrial carcinoma patients.

000205

**PROGNOSTIC FACTORS AND SURVIVAL RATE IN PATIENTS WITH EPITHELIAL OVARIAN CANCER TREATED WITH PACLITAXEL AND CARBOPLATIN**

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**Objectives:** The purpose of this retrospective study is to identify prognostic factors and survival rate in patients with epithelial ovarian cancer treated with combination chemotherapy.
**Methods:** Carboplatin and Cyclophosphamide were used in stage Ic and Paclitaxel and Carboplatin were used in stabe II to IV after primary Surgery.
**Results:** FIGO stage distribution of 98 patients were 38.2% for stage, 5.9% for stage α, 44.1% for stage β, 11.8% for stage χ. The histopathologic type distribution were serous type (45.6%), mucinous type (36.8%), endometriod type (8.8%), clear cell type (7.4%), mixed type (1.4%). In 18 patients (26.5%, residual tumor size more than 1 cm after primary cytoreductive surgery. The overall 5-year survival rate was 55.7%, and 5-year survival rate of each stage were as follow: 95.8% (stage I&II), 28.4% (stage β), 0% (stage χ). The overall survival time of stage /α were 90 months, stage β 39 months, stage χ 17 months. In multivariate analysis of prognostic factors, P value of FIGO stage, residual tumor volume, and ascitic fluid volume were calculated as follow p = 0.011, p = 0.026, p = 0.031.
**Conclusions:** Paclitaxel and Carboplatin were effective chemotherapeutic agents in stage II to IV serous ovarian cancert patients. FIGO stage, residual volume, ascitic fluid volume were most significant independent prognostic factors.

000206

**STAGE I ENDOMETRIAL CANCER:TREATMENT AND 5, 10 AND 15-YEAR SURVIVAL**

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From 1987 to 1989,192 patients with Stage I endometrial cancer were treated and follow-up in our institution. The operation-total hysterectomy and billateral adnexectomy, postoperative radiation therapy and chormonotherapy were performed. For Kaplan-Meier 5, 10 and 15-year survival were used a Software program SPSS Inc., 1989-2004. Ther is no significant differences betwen 5, 10 and 15-years survival.The 15-year survival were 78%-94% and depended of the depth of invasion and grade of the differenciation. Our data show that Stage Ia well differentiated endometrial adenocarcinoma is highly curable disease with 15-year survival of 98%.

000207

**RELATIONSHIP BETWEEN PRETREATMENT SERUM SQUAMOUS CELL CARCINOMA ANTIGEN AND CYFRA 21-1 LEVELS AND SURVIVAL IN PATIENTS WITH INVASIVE SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX**

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Objective was to determine the relationship between pretreatment serum squamous cell carcinoma antigen (SCC) and Cyfra 21-1 levels and survival in patients with invasive squamous cell carcinoma of the cervix. 131 cervical squamous cell carcinoma patients were included. Pre-treatment levels of SCC antigen and Cyfra 21-1 were measured, with a 4 year minimum follow up. 32 recurrent disease (RD) patients were compared to 99 non-recurrrent disease (NRD) patients with respect to tumor markers, FIGO stage, lesion size, lymph node status, and parametrial involvement. Statistical analysis of parameters was conducted for relationship with recurrent disease prediction and survival. Pre-treatment serum SCC antigen and Cyfra 21-1 levels were significantly higher in the RD group (P = 0.000). Combined SCC antigen and Cyfra 21-1 levels showed higher sensitivity for prediction of recurrence (90.6%). Pre-treatment SCC antigen and Cyfra 21-1 levels showed significant correlation with high FIGO stage, large lesion size, lymph node status, and parametrial involvement (p = 0.000). Normal pre-treatment levels of SCC antigen and Cyfra 21-1 showed a 5-year survival of 93% and 90% respectively, while elevated levels showed significantly decreased survival of 63% and 59%, repectively (p = 0.000). Odds ratio for cumulative survival were 6.87 for SCC antigen, and 5.07 for Cyfra 21-1, p = 0.000). Initial pre-treatment levels of serum SCC antigen and Cyfra 21-1 are closely related to FIGO stage, lesion size, lymph node and parametrial involvement in patients with squamous cell carcinoma of the cervix. Also, these markers may be independent factors in predicting recurrent disease and survival.

000208

**GENOTYPE DISTRIBUTION OF HUMAN PAPILLOMAVIRUS IN KOREAN WOMEN**

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**Objectives:** To evaluated human papillomavirus (HPV) genotype distribution and prevalence according to pathology in Korean women.
**Patients and Methods:** Women who had abnormal cytology or colposcopy was subjected to HPV test in our hospital. HPV detection and genotyping were done using commercially available kit (HPV DNAChipâ). We searched articles tested HPV genotype using HPV DNAChipâ in Korean women, and divided HPV genotype into three groups by pathology.
**Results:** A total of 1283 cases HPV genotype was detected. The most prevalent genotype in all HPV-positive cases were HPV-16 (39.5%), -58 (10.3%), -18 (7.4%), -52 (6.1%), -35 (5.5%), -33 (4.5%). In normal, HPV-16 (28.0%), -35, -52 (each 7.6%), -51, -68 (each 6.4%) were most prevalent genotype. The most frequently found genotype in cervical intraepithelial lesion (CIN) and atypical squamous (glandular) cells of undetermined significance (ASCUS/AGUS) were HPV-16 (31.3%), -58 (13.5%), -52 (7.4%), -18 (6.5%), -35 (5.6%). In cervical cancer, HPV-16 (58.3%) was the most prevalent type and -18 (9.6%), -58 (7.4%), -33 (5.6%), -35 (4.4%) were next most prevalent type.
**Conclusions:** HPV-16 was the most prevalent genotype in all cervical findings. HPV-58 was more prevalent genotype than Europe and US. But, our results are similar to that in China and Japanese. This data can be used in developing HPV vaccine for prevention of cervical cancer in Korean women.

000209

**IMPACT OF FDG-PET ON RECURRENT CERVICAL CANCER**

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Since 2001, we have enforced our multimodality team with the incorporation of nuclear medicine physicians with their expertise in positron emission tomography (PET). We hope the adding of PET, through a weekly multidisciplinary combined conference may allow a refined approach in determining and providing appropriate treatments for patients with recurrent cervical cancers. Patients and Methods After primary treatment, cervical cancer patients were followed regularly. Once a recurrence suspected, the case was presented at institutional Multi-disciplinary Gynecologic Oncology Combined Conference. Additional study, including image-guided biopsy or PET study was arranged according to the conclusion of conference discussion. Treatment was suggested in the conference and the final decision made by the physician in charge. Medical information including age, stage and histologic type at, and treatment for primary disease, date and site(s) as the first evidence of recurrence, contemporarily recognized site(s) of recurrence before combined conference, modification of disease status after the conference, treatment outcome and survival status were collected prospectively in the study group and were retrieved from medical document for the reciprocal historic control group. Results 250 patients with primary recurrent cervical cancer were presented at combined conference between February 8, 2001 and December 31, 2004. A reciprocal patient group composed of consecutive patients with recurrent cervical cancer treated before February 2001 was taken as control group. Survival outcome and curative-intent treatment delivered between groups was comprehensively compared. We will present a complete set of our data at the meeting.

000210

**SURGICAL TRAUMA AND TUMOR GROWTH, METASTASES AND SURVIVAL – AN ANIMAL MODEL**

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**Objective:** Surgery plays an important role in diseases treating, especially in cancer. The impact of surgical trauma, especially in suboptimal operations, on treatment outcome has not been adequately studied. We designed an animal model in mice with subcutaneous tumor implantation followed by surgical trauma. Material and Method: 30 BALB-C mice were used in this animal study model. 2.5*104 CT-26 colon cancer cells was injected subcutaneously without intravasation at mice's thighs in 17 of these 30 mice (Day 0). The other 13 mice were used as a control group. After 14 days of cancer cells implantation, half (9/17) of these cancer growth mice and half of the control group (7/13) underwent a traditional laparotomy at their abdomen wall without manipulation of mice's original tumor (Day 14). The original tumors were measured. The survival condition was also recorded. Serum VEGF, IL-6 and TGF-β1 were measured with ELISA kit (R&D systems Inc.).
**Result:** No statistic difference in mean tumor size between these two groups ($p = 0.683$) was noted. However, the overall survival has significant difference in Kaplan-Meier survival analysis ($p = 0.003$). IL-6 showed significantly difference between surgical group, non-surgical group and surgery without tumor implantation group ($p = 0.031$).
**Conclusion:** In this preliminary study, surgical procedures without removing all tumors in tumor growth mice may affect their survivorship compared with non-surgical group. With no difference in tumor size at primary implantation site, we speculate that the cause of survival difference maybe due to enhanced tumor metastases in the study group. Further study on this point is needed.

000211

**PATIENTS WITH MALIGNANT OR PREMALIGNANT CERVICAL LESION HAVE INCREASED RISK OF BECOMING HEPATITIS B CARRIER**

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HPV Infection is a prerequisite but insufficient for cervical carcinoma development. HPV infection and related cellular changes are mostly transient and those with persistent HPV infection have an increased risk of developing CIN and potentially cervical carcinoma. The clinical course of HPV infection is therefore similar to that of the Hepatitis B infection. That is vast majority of infected individuals would recover spontaneously while a sub-group of patients who fail to eradicate the virus would become carriers, suffer from chronic hepatitis and might develop hepatocellular carcinoma. We therefore postulate that women who develop CIN or cervical carcinoma are immunologically less competent in eradicating the viral infection. This weakness in the immune system would predispose them to become hepatitis carriers if they are infected with Hepatitis B Virus. We have collected blood from 156 patients with cervical carcinoma, 361 patients with high grade CIN and 199 women with other obstetric or gynaecological problem for this study. Patients who have been infected by Hepatitis B in the past were identified by anti-core antibody and these patients were tested for Hepatitis B surface antigen. Among the 84 patients with cervical carcinoma and 130 patients with high grade CIN that were tested for Hepatitis B surface antigen, 30.4% were positive. This figure is significantly higher than the 15.7% recorded in the 89 women without cervical malignancy or CIN. Our data therefore supported our hypothesis that patients who developed high grade CIN or cervical carcinoma have inherent weakness in their immune system.

000212

**QUANTITATIVE ANALYSIS OF HUMAN PAPILLOMAVIRUS TYPE 16 IN CERVICAL NEOPLASM**

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The study was conducted to evaluate the relation between HPV 16 viral load and the severity of cervical lesions. Study population was recruited from colposcopy and general outpatient clinic. Smears were taken for DNA extraction. The presence of HPV 16 E6 and E7 was detected using HPV 16 specific PCR reaction. The HPV 16 load in the specimens that were positive for HPV 16 specific PCR, were quantified by using real-time PCR assay. Among the 394 women recruited, 148, 121 and 125 had high grade (HG) cervical intraepithelial neoplasia (CIN), low grade (LG) CIN and normal cervix respectively. Sufficient DNA integrity was available in 347 samples. Among the 121 HPV 16 positive cases, 70 had HG CIN, 34 had LG CIN, and 17 had normal cervix. With quantitative analysis using real-time PCR, the percentages of samples with high number DNA copies were found to increase with the severity of diseases. A significant difference in DNA copies among the 3 groups could also be demonstrated (HG CIN vs. Normal, $p < 0.001$; HG CIN vs. LG CIN, $p < 0.001$). Area under ROC curve of the HG CIN vs. LG CIN and Normal was 0.836 and indicated that quantitative PCR had a good diagnostic value in differentiating HG CIN from the LG CIN and Normal group. Our data suggested evaluation of viral load might be useful in the management of patient with abnormal smear.

000213

**THE ROLE OF THE PARA-AORTIC LYMPH NODE DISSECTION IN EPITHELIAL OVARIAN CANCER**

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The aim was to investigate the incidence of nodal involvement and to identify the role of systematic para-aortic lymphadenectomy in the epithelial ovarian cancer. Between June 1995 and May 2004, 116 women with epithelial ovarian cancer who undertook optimal debulking surgery and para-aortic lymphadenectomy were investigated. Pelvic and para-aortic nodal metastases was 43.1% (50/116) and 35.3% (41/116), respectively. The frequency of LN metastases according to the stage (clinical stage I, II and III-IV) were 14.6% (6/41), 52.2 (12/23) and 75.0% (39/52), respectively. In patients with stage Ia, Ib and Ic disease, the rates of nodal involvement were 11.8% (2/17), 0% (0/2), and 18.1% (4/22), respectively. None of 2 patients with stage I and grade I had nodal involvement. None of 12 patients with mucinous tumors and of 6 patients with endometrioid tumors confined to the ovary had nodal involvement. Among 116 patients, para-aortic lymph node sampling (PALNS) was performed on 71 patients and para-aortic lymph node dissection (PALND) was performed on 45 patients. There was no significant difference in both groups with respect to patient's characteristics. But there was a significant difference in PFS in advanced stages ($p = 0.029$). The patients who undertook PALND in advanced stage showed the better PFS than the patients who undertook PALNS. Pelvic and PALND is important in surgical staging in ovary cancer, but could be omitted in patients with apparent stage I mucinous and endometrioid disease, and stage I grade I tumor. Systematic PALND may enhance PFS in advanced stages but not in early stages in the patients with optimal cytoreduction.

000214

**FISH ANALYSIS IN CERVICAL DYSPLASIC LESIONS AND SQUAMOUS CELL CARCINOMA USING TISSUE MACRO-ARRAYS**

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**Introduction:** The change in the copy number of some oncogenes has been closely related with the progression of the disease. A number of studies have shown frequent gains and losses of several specific regions, like gains in 3q, 5p, 8q, 11q, 17q and 20q, and losses in 3p, 4p, 5q and 18q. The genes involved in these regions have not been fully identified.

**Design:** The aim of the present study was to analyse of the genetic changes of the following oncogenes: c-MYC (8q24), HER2/neu (17q21) and BCL-2 (18q21), ZNF217 (20q13.2), hTERC (3q26) and hTERT (5p15), using flurescence in situ hybridization (FISH). Among 66 analysed patients, 45 were diagnosed as CIN (14 CIN I, 15 CIN II, 16 CIN III), 11 as infiltrating squamous cell carcinoma (ISCC) and 10 were cervical samples with normal epithelium.

**Results:** The results of the study are shown in the following table (% of 3 or more copies of gene).

**Conclusions:** CIN III and ISCC showed an increased number of cases with three or more copies of all the probes. In some cases these aberrations were observed together.

| | CIN I | CIN II | CIN III | ISCC |
|---|---|---|---|---|
| c-MYC | 37.5% | 71% | 50% | 100% |
| CyD1 | 30% | 46% | 75% | 72% |
| Her2/neu | 27% | 43% | 66% | 100% |
| BCL-2 | 0% | 33% | 22% | 85% |
| ZNF217 | 100% | 54% | 90% | 100% |
| hTERT | 20% | 80% | 66% | 100% |
| hTERC | 33% | 83% | 100% | 83% |

000215

**PREDICTION OF CERVICAL INVOLVEMENT IN ENDOMETRIAL CANCER BY DIFFERENT PREOPERATIVE EVALUATION METHODS: CLINICAL EXAMINATION, D&C AND HYSTEROSCOPY**

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**Objective:** Endometrial cancer with preoperatively designated cervical involvement is usually treated with radical hysterectomy, but in the absence of evidence of cervical invasion, simple hysterectomy is preferred. The aim of our study was to evaluate the ability to predict cervical involvement in endometrial cancer of three preoperative modalities: clinical examination, dilatation and curettage (D&C) and hysteroscopy.

**Patients and Methods:** The records of 114 surgically staged consecutive endometrial cancer patients treated at our institution from 1997 to 2003 were retrospectively analyzed. Preoperative staging procedures, surgical pathology reports, adjuvant treatments, follow-up and demographic data were recorded.

**Results:** Fourteen (12.2%) patients had cervical involvement (stage 2) according to the surgical pathology report. Nine (7.8%) patients were staged 2a and five (4.3%) patients were staged 2b. Clinical

evaluation by inspection and palpation had failed to reveal any clue for cervical involvement. The preoperative diagnostic procedures included hysteroscopy in eight patients, D&C in five patients and simple biopsy in one patient. All the hysteroscopy procedures did not reveal any suspicious lesion in the cervical canal. Overall out of the 14 patients only two patients (14.2%) who had the traditional fractional D&C were the only patients with preoperative evidence of cervical involvement.

**Conclusion:** Hysteroscopy and clinical examination are weak tools for the prediction of cervical involvement in endometrial carcinoma. Adding cervical canal curettage while performing either hysteroscopy or D&C can be of value in order to preoperatively properly predict cervical involvement.

000216

**ABERRANT P53 IMMUNOSTAINING AS A PROGNOSTIC FACTOR IN EPITHELIAL OVARIAN CANCER; THE IMPACT OF METHODOLOGY**

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Controversies remain on the prognostic impact of the well-known tumor suppressor gene p53 in ovarian cancer, which might be due to methodological differences between available studies.

**Aim:** To analyse and compare the prognostic impact of p53 immunostaining in two large, clinically well-defined groups of ovarian cancer patients.

**Patients and Methods:** Paraffin-embedded samples from 555 patients were collected (227 Dutch and 328 from the Scottish Gynaecological Clinical Trials Group). P53 expression was determined by immunohistochemistry (IHC) using the DO-7 antibody on tissue microarrays (TMA). TMA and IHC were performed in the same laboratory for both groups. For statistical analysis different cut-off points for aberrant p53 expression were used.

**Results:** In both groups separately as well as in the whole group P53 staining was associated with poor survival in univariate analysis, but not in multivariable analysis, while P53 staining did not predict response to chemotherapy. When using p53 staining intensity only as a factor, the prognostic impact of weak and strongly positive p53 immunostaining was similar in both groups, but significant discrepancies were observed for negative and positive p53 expression between the Dutch and Scottish series.

**Conclusion:** Although the prognostic value of strong positive p53 staining is established in this study, the role of negative and moderate immunostaining remains less clear. Differences in storage and handling of paraffin-embedded tumour samples might explain variability in outcome of prognostic factor studies.

000217

**DIAGNOSTIC VALUE OF P53 EXPRESSION IN THE STUDY OF SEROUS EFFUSIONS FROM PATIENTS WITH OVARIAN NEOPLASMS**

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**Introduction:** The diagnosis of malignancy in serous effusion can be difficult because activated mesothelial cells may resemble malignant cells mainly when the neoplasm is well differentiated or a borderline lesion. In recent years a large number of monoclonal antibodies have been evaluated in order to clarify all these problematic cases. P53 mutations are the most frequent genetic changes in human malignancies, including ovarian carcinomas. The purpose of our study was the investigation of p53 expression in body effusions borderline or low grade ovarian tumors.

**Materials and Methods:** A total of 100 peritoneal fluids and 7 pelvic washings were examined from patients with primary ovarian neoplasms. They included 13 of reactived mesothelium, 9 borderline lesions, 5 benign neoplasms and 90 ovarian carcinomas. The specimens were prerared by Liquid based Cytology and immunostained with mouse monoclonal antibody. Then, the results of immunoexpression were correlated with the cytologic diagnosis and histologic ones when available.

**Results:** The percentage of nuclear staining as well as the intensity of the stain of epithelial cells was evaluated. Moderate to strong possitivity was observed in most of the low and high grade tumors as well as in borderline lesions. No expression of p53 protein was observed in benign effusions.

**Conclusions:** The p53 overexpression represents: a) an indicator for malignancy b) combined with cytomorphology may be useful in detecting reactive mesothelium borderline or low grade ovarian carcinomas. c) Additionally, Thinprep technique offers significant advantages in the use of immunocytochemistry versus to Papanicolaou conventional method.

000218

**THE DEVELOPMENT OF SUBSPECIALITY TRAINING AS GYNAECOLOGIC ONCOLOGY TARGETING TO DEVELOPING COUNTRIES**

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**Introduction:** The subspeciality of Gynaecologic Oncology has made many contributions to women's health care management in the last few decades in the developed world. Gynaecological cancers form more than 45% of cancers in Indian women. According to the National Cancer Registry Project of the Indian Council of Medical Research, the incidence of this group of malignancies varies between 31.6 and 49.5 per 10,000 population. Cervical Cancer is the most common cancer affecting Indian Women and is the leading cause of death from cancer in women in India. However, the medical personnel who manage these patients vary in institutions all over the country. There are very few institutions in which there is a Department of Gynaecologic Oncology in India. Moreover less than forty Indian Obstetricians and Gynaecologists who have exclusively restricted themselves professionally to the subspeciality of Gynaecologic Oncology

**Materials and Methods:** The questionnaire has been formulated and distributed among the post-graduate students, Colleagues of Obstetrics & Gynaecology and other subspeciality colleagues including Medical, Surgical and Radiation oncologists and general practitioners from 2000 onwards and the opinions regarding the referral system need for 'Gynaec Onco-Wing' in Medical Colleges need for certified courses in Gynaecologic Oncology and the duration of the course. More than two thousand questionnire forms has been distributed during Continous Medical Education Programme/workshops/Conferences and to few Medical colleges.

**Results:** Majority of the participants are colleagues and postgraduate students from Obstetrics and Gynaecology and they felt that the necessity to have 'Gynaec-Onco Wing' at Medical Colleges

and to the essentiality to have two years certified courses in Gynaecologic Oncology. However it is the surgical or other oncology colleagues opined to have 6 months to one year Fellowship Courses. However, all of them felt that the 'Gynaec Oncology' is a unique subspeciality to serve the women with gynaecologic oncology.
**Conclusion:** The present survey with the questionnaire suggests that the necessity of the Development of Gynaecologic Oncology as a Subspeciality in India and other developing countries to properly manage the women suffering from gynaecological cancers. We need to formulate the criteria for their training programme, emphasising its importance to all the universities, Medical Council of India through the Organisations.

000219

**MATRIX METALLOPROTEINASE-1 PROMOTER POLYMORPHISM AND RISK OF OVARIAN CANCER**

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Matrix metalloproteinase-1 (MMP-1) plays a key role in invasion and metastasis of tumor cells by degradation of extracellular matrix. The 2G/1G single nucleotide polymorphism in the MMP-1 promoter at -1607 bp has been reported to affect the transcriptional activity. This polymorphism have been reported to associate with various cancer types. In this study, our aim was to determine if there is an association between MMP-1 gene promoter polymorphism and Turkish patients of ovarian cancer. The blood samples were collected from 42 cases of ovarian cancer and from 43 aged matched control subject. PCR and RFLP tecniques were used to determine insertion-deletion (2G/1G) polymorphism in MMP-1 promoter. The genotypes did not differ between cases and controls ($p>0.05$). Genotype frequencies were 2G/2G 78.6%; 2G/G 21.4%; G/G 0% in the patients and 2G/2G 79.1%; 2G/G 20.9%; G/G 0% in the healthy controls. We did not observed any differences with allele frequencies between ovarian cancer (89.3%) and control subjects (89.5%) for 2G allel. There was no relationship between MMP-1 genotypes and tumor behavior (invasive-borderline) or tumor stage (early-advance). Our results show that MMP-1 promoter polymorphism did not enhance the risk of ovarian cancer development and invasion in Turkish patients.

000220

**POSITIVE MARGIN OF CONIZATION: WHAT IS THE RISK FACTOR?**

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**Background:** Conization is the popular procedure in most cases of CIN III and some cases of early cervical cancer. Many reports show the conservative management of positive margin is reasonable. Nevertheless, it is generally accepted the positive margin of conization is the major cause of additional operation such as hysterectomy. The aim of this study is to evaluate the risk factors of positive margin and to reduce the positive rate.
**Patients and Methods:** 283 CIN or early cervical cancer women who underwent conization by LEEP entered this study. We evaluated many possible risk factors for positive margin, including age, weight, height, BMI, gravity, parity, abortion, severity of disease, glandular involvement, and HPV infection.
**Results:** Of the 283 patients, 80 (28.2%) had positive margin in their conization specimens (CIN 19.3%, cancer 60.7%). Statistically high significant risk factors of positive margin included older age (P-trend $< 0.001$), higher BMI (P-trend = 0.036), higher pathologic lesion (P-trend $< 0.001$), and involvement of endocervical gland (OR = 2.5, 95% CI 1.5-4.2). Parity (P-trend = 0.054) showed statistically marginal significance. Weight (P-trend = 0.154), height (P-trend = 0.456), gravity (P-trend = 0.194), abortion (P-trend = 0.813), and HPV infection (OR = 1.2, 95% CI 0.5-2.5) were not statistically significant risk factors.
**Conclusions:** The data of present study demonstrated that older age, high BMI, and higher pathologic diagnosis are high statistical risk factors of positive margin we can know preoperatively. Performing conization, it can reduce a positive rate that gynecologists consider the risk factors.

000221

**PROGESTERONE RECEPTOR-B GENE REACTIVATION IN POORLY DIFFERENTIATED ENDOMETRIAL CANCER CELLS BY EPIGENETIC MODIFICATION REAGENTS**

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**Objectives:** Poorly differentiated endometrial cancers are often progesterone receptor (PR) negative and recalcitrant to the effects of progestational therapy. Our aim was to determine if epigenetic interference using DNA methylation and histone deacetylase inhibitors could restore progesterone receptor-B (PR-B) expression in PR-B negative endometrial cancer cells.
**Methods:** PR-B mRNA, protein, and PR-B promoter DNA methylation levels were measured before and after drug treatment using real-time PCR, Western blot analysis, and methylation-specific PCR. Dose-response and duration of effect for aza-deoxycytidine (ADC) and Tricostatin A (TSA) were characterized. Cellular effects of prolonged as well as repeated drug treatment were also examined.
**Results:** Analysis of KLE and HEC-1B cell lines failed to show PR gene deletion or mutation, but hypermethylation of the PR-B promoter was present indicating that epigenetic silencing is responsible for the absent PR-B protein expression. Further supporting this, administration of ADC and TSA restored PR-B mRNA and protein expression. The effects of ADC and TSA were seen at doses as low as 0.05 uM and 0.15nM, respectively, and were synergistic, resulting in up to a 110-fold induction in PR-B mRNA levels. Sustained reactivation of PR-B mRNA and protein persisted for 48 hours after drug withdrawal, and was observed during both prolonged and repeated drug treatment.
**Conclusion:** Robust and sustainable PR-B reactivation can be achieved with low concentrations of ADC and/or TSA. These small molecule epigenetic modifying agents are currently being studied in phase II clinical trials and may be useful to sensitize PR-B negative endometrial cancer to progestational therapy.

000222

**PREOPERATIVE SERUM IGF-1 AND IGFBP-3 LEVELS IN PATIENTS WITH GYNECOLOGIC MALIGNANCIES**

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**Background:** It has been suggested that IGF and IGFBP may have a role in the development of malignancies.
**Objective:** To compare preoperative serum IGF-1 and IGFBP-3 levels in gynecological cancers prospectively.
**Patients & Methods:** A total of 66 patients with gynecological cancer (31, 22 and 13 patients with ovarian, endometrial and cervical

cancer, respectively) were prospectively evaluated with respect to preoperative serum IGF-1 (< 50 vs. >50), IGFBP-3 (< 3000 vs. >3000) and clinico-pathological variables. Chi-square and Kruskal-Wallis tests are used for the statistical evaluation.
**Results:** There were no significant differences in age of patients. Mean IGF-1 levels were 63, 108.8 and 148.6 in ovarian, endometrial and cervical cancers respectively (p = 0.001). IGF-1 levels were >50 in 51.6% of ovarian cancers while it was 81.8% and 92.3% in endometrial and cervical cancers respectively (p = 0.009). Inter-group comparison with respect to IGF-1 showed significantly low levels in ovarian cancers compared with endometrial and cervical cancers. Mean IGFBP-3 levels were 2754, 3139.2 and 3169.4 in ovarian, endometrial and cervical cancers respectively (p = 0.032). IGFBP-3 levels were >3000 in 41.9% of ovarian cancers while it was 59.1% and 76.9% in endometrial and cervical cancers respectively (p = 0.09). Inter-group comparisons with respect to IGFBP-3 levels revealed a significant difference only between ovarian and cervical cancers (p = 0.034).
**Conclusion:** IGF-1 and IGFBP-3 may have a role in the development of gynecological cancers. Role of these proteins and their prognostic significance should be investigated prospectively.

000223
**PEGYLATED LIPOSOMAL DOXORUBICINE (CAELYX®) IN HEAVILY PRETREATED PLATIN RESISTANT OVARIAN CARCINOMA: HACETTEPE EXPERIENCE**
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**Background:** Ovarian carcinoma is the most lethal female genital cancer. Despite to the agressive primary therapy including cytoreductive surgery and platin-taxol based chemotherapy, a significant rate of these patients still develop recurrent disease. Recurrent patients can be recruited to different second-line chemotherapeutics, however the optimal second line therapy is still a debate.
**Objective:** To analyze the response rates of recurrent platin resistant EOC patients to pegylated liposomal doxorubicine (Caelyx®).
**Material and Method:** Twenty-nine patients were retrospectively evaluated for their response to Caelyx salvage therapy with the regimen 50 mg/m2 per 28 days by i.v. administration. Patient responses were evaluated using serum Ca-125 levels (n = 13, 44.8%), clinical responses (n = 6, 20.7%) and radiologic findings (n = 10, 34.5%). All patients had initial staging and debulking surgeries followed by initial first line platine based chemotherapy at Hacettepe University during 2003-2005. None of the patients had platine sensitive disease.
**Results:** Mean age of the patients was 49.09 (29-69). Overall, median number of Caelyx cycles used was 4.63 (1-9). Caelyx was not the first choice among salvage therapies in any patient. It was used in second, third and ≥4. choice in six (20.7%), eleven (37.9%) and ten patients (41.4%), respectively. Of these patients, 8 (27.6%) had partial response, 5 (17.2%) had stabile disease and the remaining 16 (55.2%) had progressive disease after the Caelyx usage.
**Conclusion:** Liposomal doxorubicin is a good alternative with comparable effectivity compared to other second line chemotherapeutic agents.

000224
**COMPARISON OF CYCLOOXYGENASE-2 (COX-2) EXPRESSION IN SQUAMOUS CELL CARCINOMA AND ADENOCARCINOMA OF THE CERVIX**
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**Background:** COX-2 expression is an important factor for development and distant metastasis of non-gynecologic cancers. However, COX-2 expression correlations with clinico-pathological variables of cervical adenocarcinoma (AdenoCa) have not been investigated properly.
**Objective:** To compare COX-2 expression in Squamous cell carcinoma (SCC) and AdenoCa of the cervix.
**Material and Method:** We studied COX-2 expression in 74 women with cervical cancers, including 56 squamous cell carcinomas (SCC), and 18 adenocarcinomas (ACs), using commercially available polyclonal COX-2 antibodies on Formalin-fixed, paraffin-embedded tissues. All patients initially treated with type 3 hysterectomy plus bilateral pelvic and paraaortic lymphadenectomy.
**Results:** There were no significant differences with respect to pathological variables of the both groups. However, patients younger than 35 years of age were significantly higher in SCC group (59% vs.16%, p = 0.02). Significantly higher COX-2 expression was observed in cervical adenocarcinoma compared with SCC (39.2% vs. 72.2%, p = 0.01). We could not found a significant relationship between COX-2 expression, grade, size of the tumor, LVSI, presence of lymphatic metastasis (p>0.05). Multivariant analysis with logistic regression test using histology, LVSI, deep stromal invasion, presence of lymphatic metastasis revealed histological subtype to be only independent prognostic factor for the expression of COX-2 (p = 0.02, OR: 2.00; 95% CI: 1.12-3.58.)
**Conclusion:** Higher COX-2 expression may explain the poorer prognosis of cervical adenocarcinomas compared with SCC. Adjuvant COX-2 inhibitors may show beneficial effects in the treatment of cervical adenocarcinomas. Further clinical studies are needed to investigate these issues.

000225
**MECHANISM OF CEA RELEASE FROM ADENOCARCINOMA CELL LINE**
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Carcinoembryonic antigen (CEA) is one of the most frequently used tumor markers which is over-expressed in a variety of human cancers with epithelial origin such as colorectal, gastric, pancreatic, ovarian, lung and breast cancer. The precise mechanism by which CEA is released from the cell surface into serum in cancer patients has not been known so far. CEA is attached to the plasma membrane by a glycosylphosphatidylinositiol (GPI) anchor. There have been some evidences indicating a possible role for an enzyme involvement in CEA release from the cell surface. The GPI-anchor is a substrate for specific phospholipases. Considering these information, we have investigated the possible role of GPI-specific PI-PLD (GPI-PLD) in hydrolysis and CEA release. We have, therefore, used reverse transcription-polymerase chain reaction (RT-PCR) to verify GPI-PLD expression in some adenocarcinoma cell lines. By measuring the amount of CEA released from a CEA high producer cell line in the presence or absence of specific activators/inhibitors we have obtained evidence for the role of an endogenous GPI-PLD as the effective enzyme.

000226
**CAN WE SUBSTITUTE BRUSH CYTOLOGY FOR BIOPSY IN THE EVALUATION OF CERVICAL LESIONS UNDER THE GUIDANCE OF COLPOSCOPY?**
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In cervical cancer screening, colposcopically-directed biopsy is the gold standard method for identifying intra-epithelial and occult invasive lesions of uterine cervix. As biopsy needs special expertise and the procedure is not convenient for the patients, we sought to evaluate the colposcopically-directed brush cytology as a substitute for biopsy of cervical lesions. We studied a series of 150 women who were referred for colposcopic evaluation. Colposcopically-directed brush cytology and biopsy were performed for all patients with abnormal colposcopic findings. A total of 40 samples were excluded due to unsatisfactory report of brush cytology. Of the remained 110 samples, 34 abnormal pathology were reported in biopsy evaluations, while only 9 abnormal cytology were reported in brush cytology specimens. Brush cytology sensitivity and specificity were 26% and 97% respectively. We conclude that colposcopically-directed brush cytology is not a safe substitute for biopsy in the evaluation of cervical lesions.

000227

**INCREASED EXPRESSION OF THE EPIDERMAL GROWTH FACTOR SYSTEM IN ENDOMETRIOID ENDOMETRIAL CANCER COMPARED TO HEALTHY ENDOMETRIUM**

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**Background:** The epidermal growth factor (EGF) system consists of four receptors, and a number EGF-related peptide growth factors or ligands. The EGF system is ubiquitous in human organs, and is involved in malignant transformation. Cyclical variation of the EGF-system in human endometrium suggests a role in control of normal endometrial growth. As cancer represents abnormal growth, we hypothesise differences in the expression of the EGF system in endometrial cancer compared to normal endometrium.

**Methods:** RNA was extracted from fifty-two endometrial cancer samples (patients; age 67.6 (39.6 - 92); FIGO staging: 5 stage IA; 27 IB; 13 IC; 2 II; 4 III and 1 stage IV) and forty-two endometrial samples from 14 healthy women (controls, age 24 - 41 years). The four receptors HER1, HER2, HER3 and HER4 and the 6 ligands: epidermal growth factor (EGF), epiregulin (EPI), amphiregulin (AR), transforming growth factor alpha (TGF-α), betacellulin (BCL) and heparinbinding-EGF (HB-EGF) were analysed by real-time PCR.

**Results:** All receptors and ligands except EGF and BCL are detectable in patient and control endometrium. HER1 ($p = 0.0428$) and HER3 ($p < 0.0001$) show significantly lower expression and HER4 higher expression ($p < 0.0001$) in patient endometrium. AR ($p < 0.0001$), TGF-α ($p < 0.0001$), and HB-EGF ($p = 0.0171$) show higher expression in cancer tissue.

**Conclusions:** mRNA of all EGF-receptors and four ligands, AR, TGF-α, HB-EGF and EPI are present in endometrioid endometrial cancer. HER1, HER3 and HER4, and three ligands show significantly altered expression in cancer compared to healthy endometrium.

000228

**INCIDENCE AND MORTALITY OF GYNECOLOGICAL MALIGNANCIES AND BREAST CANCER: COMPARISON BETWEEN CROATIA AND FINLAND**

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The aim of our study was to compare incidence and mortality of the most common gynecological malignancies, including breast cancer, in Croatia and Finland. Both countries have about 5 million of inhabitants and represent a good model for implementing statistical methods. The incidence analysis of the most common female malignancies was based upon data from both National Cancer Registers reported for 1978-2001. In the observed period, a significant increase of breast cancer was registered. Cervical cancer showing a decrease in the late 1980's, also started to increase in 2000. Uterine body and ovarian cancer show a slow but continuous increase in both countries. A nation-wide screening program for cervical cancer started in Finland in 1963 and by the beginning of 1990s, resulted in a 80% decrease both in the age-adjusted incidence and mortality. On the other hand, Croatia reports a far more greater incidence of cervical cancer than Finland and EU. The incidence ratio of CIN III and invasive cervical cancer is also much more favorable in Finland than in Croatia; breast cancer incidence trends flattened in Finland in the last 20 years. The reasons for the high incidence rates of these cancers in Croatia may be found not only in the social-economic status of our population, but also in the recent war influencing such increased incidence rates. Mortality and survival rates are quite similar in both conutries, speaking in favor of the Croatian health care. However, Croatia obviously needs to improve national programs for cancer prevention.

000229

**CONSERVATIVE AND FERTILITY-SPARING SURGICAL TREATMENT OF OVARIAN CANCER: A CONTEMPORARY STRATGEY**

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The surgical treatment of choice in patients with early stage ovarian cancer is radical and includes hysterectomy and bilateral salpingoophrectomy. However, in young patients with ovarian cancer confined to a single ovary, surgical treatment could be conservative with presrvation of the uterus and contralateral ovary. Conservative surgery could be safely performed in patients with stage IA grade 1 disease. Several requirments for patients to undergoe conservative surgery: stage IA disease, young patient with low parity, cncapsulated tumor with no adesions,no invasion of the capsule, lymphatic or mesovarium, negative peritoneal washing, and close follow-up. The surgical management follows 2 patterns. First pattern,complete initial surgery;several surgical proceudres are performed including peritoneal cytology, ipsilateral oophrectomy, omentectomy, multiple peritoneal biopsies, uterine curettage, and pelvicand/or paraaortic lymphadenectomy. The second pattern, incomplete initial surgery;a restaging surgery is performed including:peritoneal cytology, ipsilateral salping-oophorectomy if not performed initially, omentectomy, multiple peritoneal biopsies, pelvic and paraaortic exploration with or without contralateralovarian biopsies, uterine curettage, and appendectomy for those with mucinous tumor. Patients are followed up very closely after surgery. Data will be presented. To conclude, conservative surgery for patients with with epithelial ovarian cancercould be considered in young patients with stage IA grade 1 disease adequately staged and desiring to preserve fertility potential. The risk of recurrence in the contra lateral ovary is low. It is recommended that radical surgery be performed when the desire of reproduction is no longer being considered.

000230

**GYNECOLOGY ONCOLOGY SUBSPECIALTY TRAINING IN BRAZIL**

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Gynecology Oncology as a subspecialty is a recent fact. The American Society was founded in 1973, the European Society in 1983, the International Society of Gynecology in 1987 and the Brazilian Society in 1997. In Brazil, a few Institutions offer Gynecology Oncology fellowship, and their curriculum program are not the same. Our objective was to describe who the Brazilian specialist is. A questionnaire was applied to 50 surgical oncologists that do gynecological-oncology specialty (GO) and 50 obstetric gynecologists (OG) in order to evaluate and compare them in respect to: type and time of training, involvement in research, surgical skill, actual practice in specialty. The median time of training was longer to GO group than OG group. The GO group received training to stage (100%), treat (100%) and palliate (88%) gynecology oncology patients, compared with 64%, 25% and 28% of OG. GO do more research and are more able than OG to do surgical procedures related to urology (98% x 34%), vascular and gastrointestinal surgery (94% x 32%), plastic surgery (78% x 10%), pelvic exenteration (94% X 6%), vulvectomy (96% x 28%). Our results suggest that despite of heterogeneous training of Brazilian gynecology-oncologists, their management abilities to conduct gynecologic cancer are better than obstetric-gynecologists, as evidenced in many researches about survival patterns in patients treated by GO.

000231

**USING MRS (MAGNETIC RESONANCE SPECTROSCOPY) FOR PHARMACOKINETICS OF CISPLATIN GIVEN AT A DAILY LOW DOSE AS A RADIOSENSITISER IN HUMAN CERVICAL CANCER TUMOURS**

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**Objective:** Radiotherapy and chemotherapy are often administered concurrently in an attempt to take advantage of postulated biochemical or molecular interactions between the two modalities. The objective of this study was to evaluate radiotherapy as a cisplatin-sensitizer in a cisplatin-esistant cervical cancer cell line.

**Methods and Methods:** 195Pt spectra were acquired at 37°C on a Bruker AMX-500, spectrometer using a broad band frequency probe. Typical conditions for 195Pt NMR at 107.28 MHz were: NS = 40 000, 90° pulse ~ 30 μs, acquisition time (AT) = 0.1 s. GROUP I: In vivo human cervical cancers were irradiated with external beam radiation at doses of 500, 1500, and 4500 cGy in a single fractionation. Twelve hours after XRT, cells were treated with a dose of cisplatin for 2 hours. Cell attachement was determined by cell counts using a MRS. GROUP II: A total of 25 patients with inoperable cervical cancer were treated by daily radiotherapy; sensitisation was obtained by administration of 5 mg cisplatin 30 min before each irradiation session. A complete kinetic profile of platinum was established after the first dose and at the end of treatment for 22 patients. Pt was quantified by MRS procedure.

**Conclusions:** The detection limit for quantifiable cisplatin derivates is estimated at 500 microM using 195Pt NMR. In addition these magnetic resonance techniques can provide useful information about the metabolisms of cisplatin in cervical cancers. The present findings suggest that a cisplatin in combination with radiation therapy may lead to a therapeutic benefit.

000232

**ROLE OF SUBOPTIMAL TREATMENT IN RESISTANCE TO CHEMOTHERAPY**

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Ovarian cancer is the leading cause of death from gynecological malignancies. Most patients are diagnosed when disease has spread beyond the pelvis with a 5-year survival of less than 20%. Patients with advanced disease initially respond to first-line therapies of cytoreductive surgery and chemotherapy consisting of a platinum analogue and Taxol. Drug resistance subsequently develops resulting in treatment failures. Our purpose was to study the expression of DNA damage genes in ovarian cancer that survive treatment with carboplatin (Carbo) and paclitaxel (Tax). Cells isolated from one patient during progression of disease were used. UL-3A was isolated at initial diagnosis, UL-3B after failure to cisplatin and paclitaxel, and UL-3C at final stages of disease. LD30, LD50 and LD70 doses were used to treat cells. DNA microarray was used to study gene expression patterns. Sensitivity to Carbo and Tax of surviving cells demonstrated both significant increase and decrease. Combination of Carbo and Tax resulted in increased resistance to both agents in UL-3B cells following treatment. Specific genes were affected by chemotherapy. MDM2 and MSH6 expression was increased with Carbo or Tax treatments while 53BP1, EXT1, H2AFL and UNG expression was decreased. Combined Carbo and Tax treatments resulted in decreased expression of ATR, CHEK1, PPM1D, PRKDC and increase in RAD1, CDS1 and ATRX. Analysis of ovarian cancer cells demonstrates specific gene expression patterns that may be involved in drug resistance. This novel approach provides information on the molecular mechanisms involved in drug resistance that can be utilized in the treatment of these patients.

000233

**NONDYSGERMINOMATOUS OVARIAN TUMORS: CLINICAL CHARACTERISTICS, TREATMENT, AND OUTCOME**

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In this study, our aim was to determine possible prognostic factors for relapse and to determine the efficacy of various treatments for managing relapse. We retrospectively reviewed 21 patients who had surgical resection of NDOGCT and received adjuvant chemotherapy. The median age at presentation was 18 years with median follow up of 20. Histologic records showed that patients had the following types of tumors: immature teratoma, mixed germ cell tumor, yolk sac tumors, and embryonal carcinoma. Initial surgery included unilateral salpingo-oophorectomy in 16 patients and cystectomy in 5 other patients. Three patients underwent a surgical laparotomy 1 to 12 months after the initial surgery. Four patients underwent debulking surgery that included total abdominal hysterectomy and bilateral salpingo-oophorectomy 1 to 6 months after the initial surgery. After the initial surgery, 13 patients immediately began to receive chemotherapy and the other 8 patients received chemotherapy at a median of 5.5 months (range, 1-40 months) after the initial surgery. Post operative chemotherapy included the following: bleomycin, etoposide, and cisplatin (n = 17); vincristin, actinomycin-D, and cyclophosphamide (n = 2); methotrexate, etoposide, and cisplatin (n = l); and cisplatin (n = l). 31% of the patients suffered a relapse after cisplatin combination chemotherapy. The median disease free survival was 40 months and the median overall survival was 50 months. The 5 year survival rate was 39%. This study indicates that there may be a role for aggressive cytoreductive surgery in advance NDOGCT, and to improve the management of relapse, we need to be looking for feasible second-line combination chemotherapy.

000234

**GENETICALLY ENGINEERED ENDOTHELIAL CELLS EXPRESSING VRL-LOADED FGFR1/TRAIL/APO-2L CAUSED APOPTOTIC-INDUCED DRUG DELIVERY (AIDD) IN CHEMORESISTANT STROMAL BREAST CARCINOMA**

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Inability of intratumoural drug delivery is the mainest cause of chemotherapy failure. In this study, we use genetically engineered endothelial cells to deliver vinorelbine by apoptosis in chemoresistant stromal breast Ca overexpressing MDR-1 and bcl-2. We genetically engineered endothelial cells expressing fusion protein FGFR1/TRAIL/Apo-2L which we loaded with vinorelbine-tartrate (VRL). After exposure to the FGFR1 ligand, FGF1 whose expression is elevated in breast tumours causes extensive and irreversible apoptosis in the VRL-loaded endothelial cells. Breast stromal Ca cells were obtained by surgical excision from a chemoresistant patient. IHC exhibited overexpression of FGF1, MDR1 and bcl-2. Post-treatment of breast Ca cells with VRL loaded FGFR1/TRAIL/Apo-2L expressing endothelial cells, we observed by transmission electron microscopy apoptosis of these endothelial cells forming drug-loaded apoptotic bodies which were phagocytosed by the breast Ca cells which exhibited irreversible D2 apoptotic signs indicating a bystander killing effect. Biochemically, we detected TRAIL/Apo-2L induced apoptosis which activated caspase-8 (FLIP) mediated proteolytic activation of caspase-3 a and tBID-mediated release of cytochrome-c and mitochondrial activation of caspase-9 forming the caspase-9/Apaf-1/cyt-c complex. Enhanced transport of vinorelbine through permeable apoptotic membranes of endothelial cells into breast Ca cells caused inhibition of bcl-2 expression. Flow cytometry exhibited cell cycle arrest at G2/M phase. MTT and BrdU assays exhibited inhibition of metabolic activity and DNA synthesis of tumour cells compared to controls. Concluding, apoptosis induced drug delivery (AIDD) has induced a bystander killing effect leading to eradication of breast ca cells by circumvention of chemoresistance caused by MDR-1.

000235

**VINORELBINE AND ANASTROZOLE INDUCE APOPTOSIS AND ANTIANGIOGENESIS IN BREAST DESMOPLASTIC STROMAL CARCINOMA POSTMENOPAUSAL PATIENTS OVEREXPRESSING ER AND ECM PROTEINS FIBRONECTIN AND TENASCIN**

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It was thought until now that the majority of breast Ca was epithelial. However, the mammary stroma becomes desmoplastic during malignant transformation which is characterised by overexpression of ECM proteins fibronectin and tenascin. Stromal tumours could circumvent detection by a mammogram due to their depth inside the breast. We obtain by surgical excision from 100 breast cancer patients tumour cells. From these tumours, 44 were epithelial, 37 were stromal and 19 were of both origins. IHC and PCR exhibited overexpression and upregulation of fibronectin, tenascin and ER. Post-treatment with anastrozole and vinorelbine-tartrate, we observed downregulation of FN, TN and ER. Flow cytometry exhibited cell cycle arrest at GG2/M due to MT depolymerization. BrdU and MTT analysis exhibited exhibition of DNA synthesis and metabolic activity in tumour cells compared to untreated controls. Furthermore, TEM exhibited D2 apoptotic signs of tumour cells characterised by lysis of plasma membrane releasing apoptotic bodies in the milieu which were phagocytosed by adjacent tumour cells leading to a bystander killing effect (BKE). Finally, due to inhibition of fibronectin which is an ECM macromolecule that is mediator of angiogenesis, we observed anti-angiogenesis with a Matrigel plug assay. Concluding, we induced apoptosis and antiangiogenesis in stromal breast Ca after the combined administration of anastrazole and vinorelbine.

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**TACCALONOLIDE AND VINORELBINE INDUCE PUMA, HYPODIPLOIDY AND MULTINUCLEATION, SUPPRESSION OF MICROTUBULE DYNAMICS, CELL CYCLE AT G2/M AND APOPTOSIS IN ADVANCED BREAST CARCINOMA**

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Low aqueous solubility of vinorelbine is a high substrate for MDR1 and MRP2 inserted in rtumoural plasma membrane. B-tubulin mutations are cross resistant to vinorelbine. We treat with vinorelbine and taccalonolide advanced mammary adenocarcinoma characterised by overexpression of bcl-2, MDR1, MRP2 and mutant b-tubulin according to PCR, WB and IHC. We use a combination of a MT depolymerizing agent such as VRL with a polymerizing agent taccalonolide which is more soluble in aqueous solvents than VRL reducing affinity for Pgp by being a poor substrate. Although these agents share the same target, they act in different ways. Post-treatment, although VRL and taccalonolide are structurally unrelated, they bind to mutually exclusive sites on the tubulin unit. After binding of MTCs to MT, there was synergistic bcl-2 phosphorylation, bax overexpression,circumvention of b-tubulin polypeptides, MDR1 and MRP2 due to high hydrophilicity of taccalonolide and p53 PUMA. Flow cytometry showed blockage of cell proliferation at the metaphase-anaphase (G2/M). There was enhancement in hypodiploid population of tumour cells, multinucleation, abberant spindle formation, nuclear convolution, suppression of MT dynamics and formation of MT bundling. Both drugs induced release of mitochondrial cyt-c. There was immunosuppression by inhibiting T-cell proliferation. BrdU and MTT exhibited inhibition of tumour cell proliferation. We observed nuclear factor kB-induced apoptosis displayed by nuclear condensation and fragmentation. Concluding, we observed synergy between taccalonolide and vinorelbine in potentiation of apoptosis in advanced breast Ca circumventing chemoresistance.

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**ANGIOGENESIS, ESTROGEN AND PROGESTERONE RECEPTOR COUNT IN TAMOXIFEN INDUCED ENDOMETRIAL PATHOLOGIES**

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**Introduction:** In the current study we tried to find out the possible mechanisms responsible for tamoxifen (TMX) induced histopathologic changes in the endometrial tissue, as well as, individual responses differing between subject, by studying angiogenesis, estrogen receptor (ER) and progesterone receptor (PR) count.
**Materials and Methods:** Endometrial biopsies were taken from 52 postmenopausal patients who used TMX more than 12 months. To define angiogenesis, ER and PR concentration in the endometrium, immunohistochemical dying with CD-31, ER and PR antibodies were performed. All the results were compared according to the endometrial pathologies, endometrial thickness and morphologic appereance.

**Results:** The mean age of the patients was 52,6 ± 8,9 years. The mean thickness of double layered endometrium was 12,3 ± 5,9 mm. The ratio of pathologic endometrial finding was 66.7% at the endometrial thicknesses equal to or above 10 mm and 45.5% below 10 mm. There was no statistical differences in CD31, ER ve PR numbers between these 2 groups. The number of CD31 dying was 14.8 + 7.8 in atrophic,inactive, proliferative and secretuar endometrium whereas this number was 22.5 + 9.4 in polyp, hyperplasia and endometrial cancer. There was significant difference of microvessel count between these 2 groups ($p = 0.003$).
**Conclusion:** In this study the correlation between endometrial thickness and morphology due to TMX effect and tissue angiogenesis, ER and PR number cannot be well established. However, the difference in microvessel count between the benign and pathologic endometrial findings may focus the attention to angiogenesis for future studies investigating nonestrogenic mechanisms of TMX.

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**THE EFFICACY OF HYPERBARIC OXYGEN THERAPY (HBOT) IN THE TREATMENT OF PELVIC RADIATION-INDUCED LATE SIDE EFFECTS**

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**Objective:** We investigated the efficacy of hyperbaric oxygen therapy in the management of patients with radiation-induced late side effects, that failed previous interventions.
**Patients and Methods:** The records of 10 patients were evaluated. The primary cancer sources were cervix (5), vagina (2), uterus (1), rectum (1) and bladder (1). All patients received a full pelvic dose of radiotherapy. Seven patients were also treated with surgery following the radiation treatment (hysterectomy-3, colectomy-1, vaginectomy-1, cystectomy-1 and exanteration-1). Five patients suffered from chronic cystitis, with 2 cases of vesico-vaginal fistula; 6 patients had chronic proctitis, with 2 cases of recto-vaginal fistulas; one patient presented with long standing open skin wound following surgery. All patients had imaging studies and biopsies to rule out active malignant disease. All patients received hyperbaric oxygen therapy with 100% oxygen, at 2 atmospheres, for 90 minutes (2ATA 90 min), each session.
**Results:** Mean patient age was 59 years (range 32 to 88). Mean time between completion of radiation therapy and onset of symptoms was 38 months (range 4 to 228). Patients received an average of 28 HBOT (range 16 to 40). Nine patients reported improvement in bladder and bowel symptoms and decrease in vaginal discharge. One patient completed treatment with symptomatic improvement, but developed lung metastasis. None of the patients reported side effects of the HBOT.
**Conclusion:** HBOT is a safe and effective treatment modality in the management of radiation-induced late side-effects, such as soft tissue necrosis, cystitis, and proctitis, in patients that other forms of management have failed.

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**A ROLE OF INFLAMMATORY DISEASES OF FEMALE GENITAL TRACT IN THE FORMATION AND PROGRESSION OF ENDOMETRIAL CANCER**

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To reveal possible interrelationships between chronic inflammatory diseases of female genital tract and endometrial carcinoma, women with histologically confirmed endometrial adenocarcinoma were examined to find signs of chronic inflammatory diseases of female genital tract. Women who were subjected to hysterectomy and in whom diagnosis of endometrial adenocarcinoma was then verified histologically ($n = 73$) were involved in the study. It was found that 57.6% of women with endometrial carcinoma had an episode of inflammatory pelvic disease in their life. In women with endometrial cancer who had an episode of inflammatory pelvic disease in their life, leukocyte infiltration in endometrial stroma of endometrial adenocarcinoma was found in 69.6% of cases, but leukocyte infiltration on cancer samples was found only in 42.9% of cases in patients who did not mention inflammatory pelvic disease in their life. Archive slides of endometrial adenorarcinoma was reviewed to find signs of inflammation. Leukocyte infiltration was found in endometrial stroma in 77% of samples with poorly differentiated endometrial adenocarcinoma, in 58.8% of samples with moderately differentiated endometrial adenocarcinoma, in 42.8% of cases in samples of well differentiated endometrial adenocarcinoma and in 33.3% of cases of atypical endometrial hyperplasia. Thus, microscopic examination showed that leukocyte infiltration in endometrial cancer samples is more often present in cancers with low degree of differentiation. Results allow to make preliminary conclusions that inflammatory response to infection plays a role in the formation of endometrial cancer and in the progression of this pathology. This work was supported by grants from RFBR (03-04-48000).

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**HISTONE DEACETYLASE INHIBITORS ENHANCE ESTRADIOL-INDUCED PROLIFERATION AND HYPERPLASIA FORMATION IN THE UTERUS OF MICE**

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It is suggested that estrogen hormones affect mechanisms that manage histone acetylation in the cell. However, it is not known how the level of histone acetylation affect estrogen-dependent processes in the uterus, especially proliferation and morphogenetic changes. Therefore, effects of histone deacetylase blockers, trichostatin A and sodium butyrate, on proliferative and morphogenetic reactions in the uterus under long-term estrogen treatment were examined. Ovariectomized mice were treated with estradiol dipropionate or vehicle and trichostatin A or sodium butyrate or with no additional treatments for a month. In animals treated with estradiol and trichostatin A or sodium butyrate, uterine mass was increased, abnormal uterine glands and atypical endometrial hyperplasia were found more often. Both histone deacetylase inhibitors enhanced proliferation (the numbers of mitotic cells and BrdU-positive cells) in luminal and glandular epithelia, in stromal and myometrial cells. Levels of estrogen receptors-alpha and progesterone receptors in uterine epithelia, stromal and myometrial cells were decreased in mice treated with estradiol with trichostatin A or sodium butyrate. Expression of beta-catenin in luminal and glandular epithelia was decreased under treatment with estradiol with trichostatin A or sodium butyrate. Both histone deacetylase inhibitors have similar unilateral effects, however the action of trichostatin A was more expressed. Thus, histone deacetylase inhibitors exert proliferative and morphogenetic effects of estradiol in the uterus. Actions of trichostatin A and sodium butyrate are associated with changes in expression of estrogen receptors-alpha, progesterone receptors and beta-catenin in the uterus. This work was supported by grant from RFBR (03-04-48000).

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**SIMULTANEOUS ESTIMATION OF THE HPV E2/E6 DNA RATIO BY MULTIPLEX PCR IN CERVICAL PRENEOPLASTIC AND NEOPLASTIC LESIONS**

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**Background:** Integration of HPV DNA into chromosomal DNA is considered an important change in the carcinogenesis of cervical epithelial cells. The viral E2 gene is often disrupted by this process, releasing the normally suppressed viral E6/E7 oncogenes, a key factor in oncogenic progression.

**Objective:** To investigate the methods for evaluating HPV E2/E6 DNA ratio by multiplex PCR in cervical preneoplastic and neoplastic lesions.

**Methods:** Simple DNA PCR and multiplex PCR were applied for the detection of an intact HPV E2, E6 gene in infected epithelial cells from the cervix with LGSL, HGSIL and invasive cervical carcinoma. 33 LGSIL (HPV16: 25, HPV18: 8), 14 HGSIL(HPV16: 9, HPV18: 5) and 12 ICC (HPV16: 8, HPV-18: 4) samples were analyzed with MPCR. The correlation between E2/E6 ratio and lesion stage was examined.

**Results:** E2/E6 DNA of HPV 6, 11, 16 and 18 were simultaneously amplified by this MPCR method. With MPCR, 2 LGSIL (HPV16: 2, HPV18: 0) [6%], 8 HGSIL (HPV16:5, HPV18: 3) [61%] and 12 ICC (HPV16: 8, HPV18: 4) [100%] samples showed low E2/E6 amplification ratio. We found that the more advanced the clinical stage, the more cases of low E2/E6 ratio there will be. This most likely suggests that the low E2/E6 ratio is correlated with cervical lesion progression.

**Conclusions:** E2 gene disruption is a likely early marker to consider in the prognostic analysis of HPV 16 and 18 chronically infected women, and multiplex PCR is a simple and sensitive method for detecting E2 gene disruption.

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**GREEN TEA POLYPHENOL POTENTIATE CYTOTOXIC EFFECTS ON CISPLATIN-CULTURED HELA CELL LINES**

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**Objective:** Green tea polyphenol (GTP) has been shown to have anti-tumor properties in a wide variety of experimental systems. In this study, we evaluated the effects of GTP on the cytotoxic effects of Cisplatin in cultured HeLa cells.

**Methods:** The HeLa cell and A549 cell lines were obtained from Korean Cell Culture Bank. GTP was extracted from tea leaves (Camellia scinensis) by water extraction and organic solvent fractionation. Cells were seeded at $1\times10^4$ cells/well in RPMI1640 media in triplicate wells on a Nunc Labware 96 well flat bottom microculture plate, with and without GTP (100 μg/ml) and at different concentrations of Cisplatin (0-1000 μg/ml). After incubating for 2 days, cell viability was determined using the MTT assay. P53 and mRNA levels in cells were determined by western blot and semiquantitative RT-PCR, respectively.

**Results:** The viability of the HeLa cells was decreased to 43% at a 600 μg/ml concentration of Cisplatin, and to 15% above 600 μg/ml as measured by the MTT assay. However, in the co-culture with GTP (100 μg/ml), the cell viability decreased to 49% at 200 μg/ml of Cisplatin and to 17% at 400 μg/ml of Cisplatin. The concentration of p53 protein and mRNA were determined 4 hours after GTP treatment. The p53 protein concentration was increased by GTP treatment, but the p53 mRNA level was not altered by GTP.

**Conclusion:** These experiments showed that GTP has a potentiating effect on Cisplatin cytotoxicity, and the increased p53 protein levels by GTP may have some role in this synergistic outcome.

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**EXTRAPERITONEAL LYMPH NODE DISSECTION IN PATIENTS WITH CERVICAL CANCER**

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**Objective:** The presence of nodal metastases is the most important prognostic factor in cervical cancer. To adjust our therapy to the true extent of the patient's disease, an extraperitoneal lymph node dissection (EPLND) was performed in all patients prior to radiotherapy (RT) or radical hysterectomy. For patients with stage I-IIa a radical hysterectomy was abandoned in case of lymph node involvement and patients received a combination of chemotherapy and RT. For patients with advanced disease the level of positive lymph nodes was evaluated to define the extent of the RT field. Patients and methods: Fifty-nine patients with cervical cancer underwent EPLND. The value of this procedure as a diagnostic tool was evaluated and treatment-related complications were monitored.

**Results:** EPLND changed the clinical management for 11 patients (31%) from a radical hysterectomy to chemotherapy/RT and for 5 patients (22%) from standard-field RT to extended-field RT. The estimated 5-year overall survival was 64%, lymph node involvment was the only significant independent prognostic factor for the 5-year overall survival (p = 0,04). The most common side-effect related to EPLND was the formation of lymph cysts in 7 patients (12%). Two patients with the combination of EPLND and radical hysterectomy developed a severe ileus postoperatively. The treatment approach of EPLND and chemotherapy/RT was without WHO grade 3 and 4 toxicity.

**Conclusion:** Our data support surgical staging by EPLND to individualize the treatment for patients with cervical cancer. The complication rate was low.

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**TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY (TYPE III) WITH PARAAORTIC & PELVIC LYMPHADENECTOMY. A RECENTLY REPORTED CASE IN A GREEK TERTIARY CENTER**

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Background: The role of laparoscopy in the management of abdominopelvic malignancies is evolving. Data from new randomized and nonrandomized controlled trials demonstrate that laparoscopic surgical staging has equal efficacy (lymph node counts, disease free survival) compared to traditional open cases and can be safely performed in selected patients

**Materials and Methods:** We report a recent, in our country, case of laparoscopic radical hysterectomy and lymphadenectomy performed in a tertiary center in a 44 yo G1P1 female with squamous cell carcinoma of the cervix, stage IIA. After a thorough preoperative assessment, informed consent was obtained and a surgical team, with experience in laparoscopic surgical staging, was assembled and performed the surgery.

**Results:** A laparoscopic radical hysterectomy type III with para-aortic and pelvic lymphadenectomy was carried out. Nineteen nodes were retrieved two of which (2/19) were positive for metastasis. She suffered a left lower extremity venous thrombosis for which she underwent standard DVT treatment with parenteric heparin and eventually oral coumadin. The patient required only one (1) analgesic suppository for postoperative pain control and remained afebrile throughout her hospitalization. She received adjuvant chemoradiation due to risk factors and is now under a standard surveillance schedule.

**Conclusion:** The performance of this procedure in a tertiary center in our country supports the fact that laparoscopic surgical staging, is gaining steadily wide acceptance by both patients and physicians, throughout the world. To our knowledge a total laparoscopic radical hysterectomy with bilateral para-aortic and pelvic lymphadenectomy has not been previously described in our country.